APPENDIX A

UNITED STATES COURT OF APPEALS,
FEDERAL CIRCUIT

Nos. 03-1285, 03-1313

SMITHKLINE BEECHAM CORPORATION and
Beecham Group, P.L.C.,
Plaintiffs-Appellants,

v.

APOTEX CORP., Apotex, Inc., and TorPharm, Inc.,
Defendants-Cross Appellants.

DECIDED: April 8, 2005
Rehearing En Banc Denied June 15, 2005

Before RADER, BRYSON, and GAJARSA, *Circuit Judges*. *

Opinion for the court filed by *Circuit Judge* RADER. Concurring opinion filed by *Circuit Judge* GAJARSA.

RADER, *Circuit Judge*.

Following a bench trial, the United States District Court for the Northern District of Illinois determined that the generic paroxetine hydrochloride anhydrate product to be produced by Apotex Corp., Apotex, Inc., and TorPharm, Inc. (collectively Apotex) will not infringe claim 1 of U.S. Patent No.

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* Pursuant to an order issued by this court *en banc*, the present opinion replaces this panel's prior opinion entered on April 23, 2004, as amended April 28, 2004, and reported at 365 F.3d 1306 (Fed.Cir.2004).

4,721,723 ('723 patent) owned by SmithKline Beecham Corp. and Beecham Group, P.L.C. (collectively SmithKline). *SmithKline Beecham Corp. v. Apotex Corp.*, 247 F.Supp.2d 1011, 1052 (N.D.Ill.2003). Based on this court's revision of the trial court's erroneous claim construction, Apotex's product would infringe claim 1 of the '723 patent. Nonetheless, because claim 1 of the '723 patent is invalid as anticipated under 35 U.S.C. § 102(b), this court affirms the district court's judgment in favor of Apotex.

I.

In the late 1970s, a British company, Ferrosan, invented a new class of compounds, including a compound that became known as paroxetine. *See* U.S. Patent No. 4,007,196 ('196 patent). The '196 patent claims paroxetine and its salts and discloses their antidepressant properties. Ferrosan eventually developed a process to produce the crystalline hydrochloride salt of paroxetine, or paroxetine hydrochloride (PHC). In 1980, Ferrosan licensed the '196 patent and its other PHC-related technology to SmithKline. SmithKline began manufacturing PHC in its Harlow plant in England.

In March 1985, Alan Curzons, a chemist in SmithKline's Worthing, England laboratory, discovered a new crystalline form of PHC while attempting to improve PHC production. Curzons's test results established that the new product was the hemihydrous form of PHC (PHC hemihydrate). Ferrosan's original form was anhydrous PHC (PHC anhydrate). PHC anhydrate comprises crystals of PHC without bound water molecules. PHC hemihydrate comprises PHC crystals with one bound water molecule for every two PHC molecules. PHC hemihydrate proved more stable, and thus more easily packaged and preserved, than PHC anhydrate.

SmithKline filed a patent application in the British Patent Office on October 25, 1985 relating to "crystalline paroxetine hydrochloride, its preparation and its uses as a therapeutic

agent." The British application identified the invention as both the hemihydrate and the anhydrate form of PHC, as well as mixtures that contain a major portion of either form. One year later, on October 23, 1986, SmithKline filed a U.S. application claiming priority to the British application that issued as the '723 patent in 1988. The '723 patent does not claim PHC anhydrate and does not claim mixtures of the two PHC forms. The only claim at issue in this case is claim 1, which reads in its entirety: "Crystalline paroxetine hydrochloride hemihydrate."

In 1993, after completing the necessary FDA approval process, SmithKline placed its antidepressant drug with PHC hemihydrate as the active ingredient on the market under the name Paxil®. In 1998, TorPharm, Inc., an Apotex affiliate and manufacturer of Apotex's generic antidepressant, filed an Abbreviated New Drug Application (ANDA) with the FDA, under 21 U.S.C. § 355(j), seeking approval to market its own PHC antidepressant drug. Apotex identified the active ingredient in its antidepressant as PHC anhydrate. Apotex's ANDA included a paragraph IV certification, *see* 21 U.S.C. § 355(j)(2)(A)(IV), that indicated Apotex's intent to market the drug before the expiration of the '723 patent because its drug would not infringe that patent.

In 1998, SmithKline initiated this infringement action against Apotex under 35 U.S.C. § 271(e)(2) on the basis of Apotex's ANDA filing. SmithKline alleges that Apotex's proposed drug will infringe claim 1 of the '723 patent. SmithKline does not allege that claim 1 of the '723 patent covers PHC anhydrate. After all, PHC anhydrate—the Ferrosan discovery—is prior art for the '723 patent. SmithKline asserts that Apotex will infringe by manufacturing PHC anhydrate tablets that necessarily contain, by a conversion process discussed below, at least trace amounts of PHC hemihydrate.

The parties filed various summary judgment motions, including cross motions for summary judgment that claim 1 of

the '723 patent was invalid (or valid) under 35 U.S.C. § 102(b) for an impermissible public use. The § 102(b) motions acknowledged that clinical trials occurred more than one year before SmithKline's filing date for the '723 patent, but disputed whether those tests qualified for the experimental use negation. The district court denied Apotex's motion and granted SmithKline's motion, holding that the '723 patent was not invalid for public use under § 102(b). The district court reasoned that the clinical trials qualified as experimental uses. *See SmithKline Beecham Corp. v. Apotex Corp.*, 286 F.Supp.2d 925, 932-38 (N.D.Ill.2001).

The district court then held a bench trial to determine the proper interpretation of claim 1 and to resolve the remaining infringement and validity issues. On the question of claim construction, the district court limited claim 1 to PHC hemihydrate in commercially significant amounts. *SmithKline Beecham Corp.*, 247 F.Supp.2d at 1030. The trial record contained uncontested testimony that a PHC anhydrate-hemihydrate mixture would need to possess a percentage of PHC hemihydrate in the "high double digits" if the hemihydrate component were to contribute any commercial value. *Id.* The district court imported that commercial significance into the claim and held that Apotex's proposed PHC drug will not infringe claim 1 of the '723 patent. The district court found, as a factual matter, that Apotex's PHC anhydrate tablets will not contain commercially significant amounts of PHC hemihydrate and rejected SmithKline's evidence to the contrary. *Id.* at 1031-39. The trial court also determined that claim 1 is not invalid.

SmithKline contested the district court's claim interpretation noting that claim 1 is clear on its face and encompasses PHC hemihydrate in any amount, however small or insignificant. In rejecting that proposed claim interpretation, the district court also opined that SmithKline's proposed construction would render claim 1 indefinite. The district court rea-

soned that SmithKline's interpretation would place potential infringers in the untenable position of never knowing whether their product infringes because even a single undetectable crystal of PHC hemihydrate would infringe. *Id.* at 1029-30.

To show that manufacture of PHC anhydrate tablets necessarily creates PHC hemihydrate, SmithKline proffered expert testimony on the so-called "seeding" or "disappearing polymorph" theory. Under this theory, Ferrosan may have originally created a crystalline compound, namely PHC anhydrate, in a relatively unstable form. For presently unknown reasons, the PHC anhydrate "morphed" into a more stable form, namely the PHC hemihydrate discovered in SmithKline's facilities. With this new form or polymorph in existence, SmithKline's experts explained, the general environment became "seeded" with crystals of PHC hemihydrate. In this seeded environment, the PHC anhydrate converts to the PHC hemihydrate upon its inevitable contact with seeds of PHC hemihydrate. In other words, the creation of pure PHC anhydrate became extremely difficult, if not impossible; the old polymorph, PCH anhydrate, has effectively disappeared in its pure form because it changes naturally into the new polymorph, PCH hemihydrate.

SmithKline's experts applied the "disappearing polymorph" theory to show that Apotex's PHC anhydrate tablets inevitably convert to hemihydrate when combined with moisture, pressure, and practically ubiquitous PHC hemihydrate seeds. The district court found that SmithKline's evidence on the "seeding" and the "disappearing polymorph" theories supported the inference that Apotex's PHC anhydrate tablets will contain at least trace, even if undetectable, amounts of PHC hemihydrate. *Id.* at 1042-43. Thus, under SmithKline's claim construction, the district court held that Apotex's PHC anhydrate drug would infringe claim 1 of the '723 patent. *Id.*

Alternatively, if claim 1 was construed to cover any amount of PHC hemihydrate and was, therefore, infringed,

the district court purported to create a new equitable defense to infringement in favor of Apotex. *Id.* at 1043-45. Under this new defense, SmithKline was responsible for producing the hemihydrate, which, by virtue of SmithKline's "disappearing polymorph" theory, seeded the environment. Consequently, SmithKline caused the alleged infringement. The district court reasoned that Apotex should enjoy the right to practice the prior art by manufacturing PHC anhydrate. Accordingly, under its alternative equitable defense, the district court absolved Apotex of liability for the consequences of SmithKline's own conduct that rendered the practice of the prior art impossible without infringing the '723 patent. The district court also held that its inherent equitable powers and the equitable nature of injunctions in general placed the injunction mandated by 35 U.S.C. § 271(e)(4)(A) within the discretion of the district court. *Id.* at 1045-52.

SmithKline also sought to assert a claim of induced infringement against Apotex on the theory that PHC anhydrate tablets convert to PHC hemihydrate in the stomach of a patient due to the increased humidity and pressure present inside the stomach. *Id.* at 1014-15. The district court excluded SmithKline's evidence on this issue, finding that SmithKline would likely not meet its burden of showing "gastrointestinal infringement." *Id.* at 1014-15. Finally, the district court considered other alternative claim constructions, which would allow claim 1 to cover PHC hemihydrate in amounts detectable either by methods available at the time the '723 patent was filed or by any means that later became available. *Id.* at 1052. The record shows that SmithKline presented the results of tests on various samples of Apotex tablets. These tests showed PHC hemihydrate in the Apotex product. The district court rejected this evidence as unreliable, mainly because SmithKline's counsel excluded certain tablets from the testing without reasonable explanation. *Id.* at 1032-42. The trial court found these excluded tablets to represent the product Apotex would manufacture upon ANDA approval. *Id.* Ac-

cordingly, the district court held that SmithKline did not prove that Apotex's tablets will contain any detectable amount of PHC hemihydrate.

SmithKline presents five arguments on appeal. First, the district court erred in limiting claim 1 to commercially significant amounts of PHC hemihydrate. Second, contrary to the district court's ruling, a claim construction that covers PHC hemihydrate in any amount does not render claim 1 indefinite. Third, the district court erred in creating an equitable defense to infringement based on SmithKline's contribution to causing the infringement. Fourth, the district court erred in holding that the injunctive relief required under 35 U.S.C. § 271(e)(4) is within the district court's discretion. Fifth, the district court abused its discretion in excluding SmithKline's evidence of induced infringement.

In its cross-appeal, Apotex argues that the district court erred in granting summary judgment that SmithKline's clinical tests qualified as an experimental use. In particular, Apotex asserts that claim 1 of the '723 patent is invalid for public use under 35 U.S.C. § 102(b) as a matter of law. This court has jurisdiction over these appeals under 28 U.S.C. § 1295(a)(1).

II.

Standards of Review

This court reviews summary judgments without deference. *See Beech Aircraft Corp. v. EDO Corp.*, 990 F.2d 1237, 1245 (Fed.Cir.1993). Of course, a denial of summary judgment, by itself, is not a final judgment amenable to appeal like a grant of summary judgment. However, when both parties move for summary judgment, each motion "must be independently assessed on its own merit." *California v. United States*, 271 F.3d 1377, 1380 (Fed.Cir.2001). In such circumstances, this court reviews summary judgment under the standard rules of FED. R. CIV. P. 56.

In this case, both parties sought summary judgment; the district court granted one and denied the other. Thus, the record shows that the parties conceded, and the district court found, that no material factual issues remain in dispute. *See Beech Aircraft*, 990 F.2d at 1245. If this court determines that no material facts remain in dispute, it may proceed to determine entitlement to judgment under the law. *See Eli Lilly & Co. v. Barr Labs., Inc.*, 251 F.3d 955, 962 (Fed. Cir.2001) ("[R]eversal is required if the district court 'engaged in a faulty legal analysis in applying the law to the facts and a correct application of the law to those facts might bring a different result.'" (quoting *Litton Indus. Prods., Inc. v. Solid State Sys. Corp.*, 755 F.2d 158, 164 (Fed.Cir.1985))); *see also Anderson v. Liberty Lobby Inc.*, 477 U.S. 242, 248, 106 S.Ct. 2505, 91 L.Ed.2d 202 (1986).

This court reviews a district court's judgment following a bench trial for errors of law or clearly erroneous findings of fact. *See Allen Eng'g Corp. v. Bartell Indus., Inc.*, 299 F.3d 1336, 1343-44 (Fed.Cir.2002). Patent infringement proceeds under a two-step analysis. First, the court interprets the claims to determine their proper scope and meaning. *See Cybor Corp. v. FAS Techs., Inc.*, 138 F.3d 1448, 1454 (Fed.Cir.1998) (*en banc*). Next, the court measures the accused product or process against the standard of the properly interpreted claims. *Id.*

This court reviews claim construction without deference. *See Markman v. Westview Instruments, Inc.*, 52 F.3d 967, 979 (Fed.Cir.1995) (*en banc*), *aff'd*, 517 U.S. 370, 116 S.Ct. 1384, 134 L.Ed.2d 577 (1996). This court reviews the second step, measurement of the accused product or process against the claim, as a question of fact. *See Allen Eng'g*, 299 F.3d at 1343-44; *Gen. Mills, Inc. v. Hunt-Wesson, Inc.*, 103 F.3d 978, 981 (Fed.Cir.1997). The review of indefiniteness under 35 U.S.C. § 112, paragraph 2, proceeds as a question of law without deference. *See Solomon v. Kimberly-Clark Corp.*,

216 F.3d 1372, 1377 (Fed.Cir.2000); *Personalized Media Communications, LLC v. Int'l Trade Comm'n*, 161 F.3d 696, 702 (Fed.Cir.1998).

Factual Findings

As an initial matter, this court holds that the record, for the most part, supports the district court's factual findings. In particular, the district court did not clearly err in concluding that Apotex's PHC anhydrate product will include trace amounts of PHC hemihydrate based on the record evidence that the anhydrate form inevitably changes into the hemihydrate form. *See SmithKline Beecham Corp.*, 247 F.Supp.2d at 1019-23.

The district court also did not clearly err in finding that Apotex's anhydrate product will not contain detectable quantities of PHC hemihydrate because SmithKline selectively tested the Apotex samples without explaining its reasons for excluding some Apotex products from the examination. Specifically, the district court's discretionary exclusion of SmithKline's unreliable evidence on this issue does not render the subsequent factual finding clearly erroneous.

Although the district court clearly accepts as true the theories of "disappearing polymorphs" and "seeding," it did not make findings of fact regarding precisely how or when PHC hemihydrate first came into existence. Indeed, traces of PHC hemihydrate in PHC anhydrate pills were not detectible in amounts less than five percent before 1985. However, Curzons undisputedly made his serendipitous discovery of PHC hemihydrate while making PHC anhydrate presumably pursuant to the teachings of the '196 patent. Moreover, although Curzons does not claim to have discovered PHC hemihydrate until March 1985, further review of samples of SmithKline's PHC anhydrate revealed that SmithKline's Harlow plant had unwittingly made PHC hemihydrate as early as December 1984. These undisputed facts conclu-

sively establish that PHC anhydrate made in accordance with the '196 patent converts into PHC hemihydrate both with and without seeding. Accordingly, this court decides the legal issues in this appeal against the factual background as determined by the district court.

Claim Construction & Indefiniteness

Claim interpretation requires the court to ascertain the meaning of the claim to one of ordinary skill in the art at the time of invention. *ResQNet.com, Inc. v. Lansa, Inc.*, 346 F.3d 1374, 1378 (Fed.Cir.2003); *Phillips Petroleum Co. v. Huntsman Polymers Corp.*, 157 F.3d 866, 871 (Fed.Cir.1998). This task requires the court to place the claim language in its proper technological and temporal context. The best tools for this enterprise are the various forms of intrinsic evidence and, when appropriate, extrinsic evidence. *See Vitronics, Corp. v. Conceptronic, Inc.*, 90 F.3d 1576, 1582 (Fed.Cir.1996). The intrinsic evidence, "i.e., the patent itself, including the claims, the specification and, if in evidence, the prosecution history . . . is the most significant source of the legally operative meaning of disputed claim language." *Id.*

Of course, at all times, the language of the claims governs their scope and meaning. *See Dow Chem. Co. v. Sumitomo Chem. Co.*, 257 F.3d 1364, 1372 (Fed.Cir.2001). Unless the intrinsic evidence compels a contrary conclusion, the claim language carries the meaning accorded those words in the usage of skilled artisans at the time of invention. *See id.*; *Vitronics*, 90 F.3d at 1582.

As stated earlier, claim 1 of the '723 patent reads: "Crystalline paroxetine hydrochloride hemihydrate." This language is not ambiguous but rather describes a very specific compound. The record repeatedly shows that artisans in this area of technology at the time of invention would have understood that the claim embraces PHC hemihydrate without further limitation.

The inquiry proceeds to the remainder of the intrinsic record to determine if the patent applicant gave these unambiguous words some unexpected definition. The district court limited claim 1 to commercially significant amounts of PHC hemihydrate. The trial court found support for this limitation in portions of the '723 patent that discuss the pharmaceutical and commercial properties of PHC hemihydrate. *SmithKline Beecham Corp.*, 247 F.Supp.2d at 1029-30. For example, the specification discusses the superior handling properties of the hemihydrate form that improve the manufacture of PHC. Those references, however, do not redefine the compound in terms of its commercial properties, but emphasize that the new compound exhibits favorable characteristics. A description of characteristics does not redefine a compound with an established and unambiguous structural definition.

Moreover, nothing in the '723 patent limits that structural compound to its commercial embodiments. Rather, the '723 specification discloses PHC hemihydrate as a compound without reference to its commercial applications. For example, the specification states that the "present invention provides crystalline paroxetine hydrochloride hemihydrate as a novel compound." '723 patent, col. 1, ll. 57-58. Furthermore, nothing in the prosecution history of the '723 patent defines the invention in terms of commercially significant quantities. Thus, reading claim 1 in the context of the intrinsic evidence, the conclusion is inescapable that the claim encompasses, without limitation, PHC hemihydrate—a crystal form of paroxetine hydrochloride that contains one molecule of bound water for every two molecules of paroxetine hydrochloride in the crystal structure.

The district court openly discussed the policies that led to its insertion of commercially significant quantities as a limitation on the meaning of the claimed compound. *SmithKline Beecham Corp.*, 247 F.Supp.2d at 1028-30. The district court observed that a claim construction that covers trace amounts

of PHC hemihydrate would likely preclude attempts to make the prior art PHC anhydrate compound. *Id.* After explaining the "*in terrorem* effect" of such a "broad" claim construction, the district court rejected the literal scope of claim 1 because it would produce "absurd results" and would "not serve any policy of patent law." *Id.* Claim construction, however, is not a policy-driven inquiry. As stated earlier, it is a contextual interpretation of language. The scope of patent claims can neither be broadened nor narrowed based on abstract policy considerations regarding the effect of a particular claim meaning. *See Quantum Corp. v. Rodime, PLC*, 65 F.3d 1577, 1584 (Fed.Cir.1995) ("[I]t is well settled that no matter how great the temptations of fairness or policy making, courts do not redraft claims."). For this precise reason, this court has repeatedly stated that a court must construe claims without considering the implications of covering a particular product or process. *See NeoMagic Corp. v. Trident Microsys. Inc.*, 287 F.3d 1062, 1074 (Fed.Cir.2002); *SRI Int'l v. Matsushita Elec. Corp.*, 775 F.2d 1107, 1118 (Fed. Cir.1985).

The district court also justified its commercial-significance limitation to preserve the claim's validity in the face of a challenge to its definiteness under § 112, second paragraph. In essence, the district court considered the claim indefinite if construed to cover undetectable trace amounts of PHC hemihydrate. In other words, the trial court feared that potential infringers would not be able to determine (and avoid) infringement if they cannot detect the claimed compound. *See Morton Int'l, Inc. v. Cardinal Chem. Co.*, 5 F.3d 1464, 1469-70 (Fed.Cir.1993). This reasoning misses the proper purpose of the definiteness requirement.

The second paragraph of § 112 requires the specification of a patent to "conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention." 35 U.S.C. § 112, ¶ 2 (2000). To satisfy this requirement, the claim, read in light of

the specification, must apprise those skilled in the art of the scope of the claim. *See Miles Labs., Inc. v. Shandon, Inc.*, 997 F.2d 870, 875 (Fed.Cir.1993). Moreover, claims need not "be plain on their face in order to avoid condemnation for indefiniteness; rather, what [this court has] asked is that the claims be amenable to construction, however difficult that task may be." *Exxon Research & Eng'g Co. v. United States*, 265 F.3d 1371, 1375 (Fed.Cir.2001). In this case, the claim covers a definite chemical structure. To a chemist in this field, this claim is plain on its face. Thus, claim 1 of the '723 patent cannot be invalid for indefiniteness under § 112.

In *Morton*, this court affirmed a district court's judgment of indefiniteness because "one skilled in the art could not determine whether a given compound was within the scope of the claims." 5 F.3d at 1470. Thus, the claims at issue were "not sufficiently precise to permit a potential competitor to determine whether or not he is infringing." *Id.* The *Morton* case, therefore, does not hold that the inability to detect the claimed compound in the infringing device renders a compound claim indefinite. Rather, *Morton* stands for the unremarkable proposition that a compound claim, to be definite, must apprise a skilled artisan of the bounds of the claim. The record in *Morton* contained "considerable evidence showing that those skilled in the art could not make the claimed compounds using the procedures of the specification, and no evidence that such compounds even exist." *Id.* at 1469-70.

This case bears little similarity to *Morton*. Here, claim 1 unambiguously identifies the bounds of the claim. It states: "Crystalline paroxetine hydrochloride hemihydrate." Thus, this claim recites in clear terms a discernible chemical structure. It would be difficult to imagine a more clear and definite claim.

The test for indefiniteness does not depend on a potential infringer's ability to ascertain the nature of its own accused

product to determine infringement, but instead on whether the claim delineates to a skilled artisan the bounds of the invention. In this case, the problem for Apotex is that it cannot accurately ascertain the nature of its own product. The scope of this claim is clear; the infringement of the Apotex product is not. Even if a claim is broad enough to embrace undetectable trace amounts of the claimed invention, "[b]readth is not indefiniteness." *In re Gardner*, 57 C.C.P.A. 1207, 427 F.2d 786, 788 (CCPA 1970). Stated more precisely, this claim is neither broad nor narrow, but definitive of this particular chemical structure. For inventing and disclosing this structure, the inventor enjoys the exclusive right to practice that invention for the patent's limited term. Accordingly, claim 1, as construed above, is not indefinite under 35 U.S.C. § 112, second paragraph.

Infringement and Equity

Having interpreted claim 1 to cover PHC hemihydrate without further limitation, this court turns to infringement. In anticipation of this very scenario, the district court performed a factual infringement analysis based on this correct claim construction. The district court held that the evidence showed that Apotex's PHC anhydrate tablets would contain trace amounts of PHC hemihydrate. *SmithKline Beecham Corp.*, 247 F.Supp.2d at 1043. As indicated above, the record supports this factual finding. This court, therefore, affirms the district court's finding that Apotex's product will infringe under this court's claim construction.

Because Apotex seeks to practice the prior art, and because that practice infringes, the next logical inquiry involves anticipation. That is, if the prior art infringes now, logically the prior art should have anticipated the claim before the filing of the '723 patent. *See Bristol-Myers Squibb Co. v. Ben Venue Labs., Inc.*, 246 F.3d 1368, 1378 (Fed.Cir.2001) (restating the axiom that "that which would literally infringe if later in time anticipates if earlier"). At trial, Apotex as-

serted that Ferrosan's process of making PHC anhydrate inherently resulted in trace amounts of the hemihydrate prior to the '723 patent and thus inherently anticipated that patent. The district court, however, determined that Apotex did not present clear and convincing evidence of inherent anticipation. According to the district court's findings, "no one knows when the hemihydrate form of paroxetine came into existence, although it is a reasonable inference that it did not exist in a detectable amount until" SmithKline's "serendipitous" discovery. *SmithKline Beecham Corp.*, 247 F.Supp.2d at 1022, 1025. Apotex does not dispute that PHC hemihydrate was first detected by Curzons in 1985, or that it is unable to prove precisely when PHC hemihydrate came into existence.

SmithKline argues that practicing the '196 patent infringes claim 1 of the '723 patent, but that the '196 patent does not anticipate claim 1 of the '723 patent. SmithKline uses the "disappearing polymorph" theory to justify its apparently inconsistent positions. On the one hand, SmithKline asserts that the creation of a prior art compound will result in a product containing at least trace amounts of their patented compound. On the other hand, SmithKline contends that the creation of the prior art compound before SmithKline's discovery of its compound did not have the same result. For this reason, the district court was understandably uncomfortable about allowing claim 1 to embrace its literal scope. The district court feared such a construction would result in "a considerable extension in the effective patent term of paroxetine because it might become difficult or even impossible to manufacture the pure anhydrous form after the Ferrosan patent expired." *Id.* at 1019. While these concerns are certainly legitimate, claim construction, as noted before, proceeds independent of its policy implications. Fortunately, the district court had the foresight to consider alternative analyses in this unique situation.

The district court, in its alternative infringement analysis, properly found infringement, but created a new equitable defense to shield Apotex from liability for that infringement. *Id.* at 1043-45. In short, the defense would apply where the patentee significantly contributed to causing the infringement. After all, SmithKline's creation of the hemihydrate form of PHC created a seeded environment that, under the facts found by this district court, makes the practice of the prior art an infringement, while arguably precluding the operation of anticipation by inherency. In this unique and unprecedented circumstance, the trial court understandably reached out to find an equitable remedy to protect Apotex. In any event, notwithstanding the potential merit of a new equitable doctrine in this unprecedented instance, this court can resolve this case without its application because claim 1 is invalid as inherently anticipated under 35 U.S.C. § 102(b). Accordingly, this court declines to address the trial court's proposed equitable defense.

The concurring opinion seeks to remedy the perceived inequity in this case by applying 35 U.S.C. § 101, arguing the subject matter of claim 1 does not cover patentable subject matter. Unfortunately, the concurrence confuses patent eligibility under § 101 with patentability under other provisions in the Patent Act, such as 35 U.S.C. § 102. The concurrence admits that PHC hemihydrate is a synthetic, man-made compound eligible for patent protection. In fact, the claimed invention is without question a "composition of matter" or an article of "manufacture" within the terms of § 101. Accordingly, the claimed invention represents subject matter eligible for patent protection under § 101. With that conclusion, the inquiry under § 101 ends.

The concurring opinion, however, would expand the subject matter eligibility analysis under § 101 to encompass some review of the scope of the claims. To the contrary, "[e]ither the subject matter falls within Section 101 or it does

not." *Animal Legal Def. Fund v. Quigg*, 932 F.2d 920, 930 (Fed.Cir.1991). The scope of the claims is not relevant to subject matter eligibility. Subject matter does not take on a different eligibility status with adjustments in the scope of the proposed claim. Patent eligibility under § 101 is simply not an issue in this case.

Anticipation—§ 102(b)

A patent claim is not valid if "the invention was patented or described in a printed publication in this . . . country . . . more than one year prior to the date of the application for patent in the United States. . . ." 35 U.S.C. § 102(b) (2000). For prior art to anticipate a claim "it must be sufficient to enable one with ordinary skill in the art to practice the invention." *Minn. Mining & Mfg. Co. v. Chemque, Inc.*, 303 F.3d 1294, 1301 (Fed.Cir.2002) (citing *In re Borst*, 52 C.C.P.A. 1398, 345 F.2d 851, 855 (CCPA 1965)). "Whether a prior art reference is enabling is a question of law based upon underlying factual findings." *Id.* (citing *Crown Operations Int'l Ltd. v. Solutia, Inc.*, 289 F.3d 1367, 1376 (Fed. Cir.2002)). Anticipation is a question of fact. *See id.* However, without genuine factual disputes underlying the anticipation inquiry, the issue is ripe for judgment as a matter of law.

The '196 patent is undisputed prior art under 35 U.S.C. § 102(b), even though the '196 patent discloses how to make PHC anhydrate and does not discuss PHC hemihydrate. PHC hemihydrate was not ...en discovered until years after the '196 patent was filed. Nonetheless, the '196 patent anticipates claim 1 of the '723 patent because the '196 inherently discloses PHC hemihydrate.

This court recently set forth the standards for anticipation by inherency:

> A patent is invalid for anticipation if a single prior art reference discloses each and every limitation of the

> claimed invention. *Lewmar Marine, Inc. v. Barient Inc.*, 827 F.2d 744, 747 (Fed.Cir.1987). Moreover, a prior art reference may anticipate without disclosing a feature of the claimed invention if that missing characteristic is necessarily present, or inherent, in the single anticipating reference. *Continental Can Co. v. Monsanto Co.*, 948 F.2d 1264, 1268 (Fed.Cir.1991).

Schering Corp. v. Geneva Pharms., Inc., 339 F.3d 1373, 1377 (Fed.Cir.2003). In *Schering Corp.*, this court also decided that the doctrine of inherent anticipation applies to the entire claimed subject matter just as it does to a single claimed feature. *Id.* at 1379 ("Because inherency places subject matter in the public domain as well as an express disclosure, the inherent disclosure of the entire claimed subject matter anticipates as well as inherent disclosure of a single feature of the claimed subject matter."). Moreover, this court reiterated in *Schering Corp.* that inherent anticipation does not require a person of ordinary skill in the art to recognize the inherent disclosure in the prior art at the time the prior art is created. *Id.* at 1377 (citing *In re Cruciferous Sprout Litig.*, 301 F.3d 1343, 1351 (Fed.Cir.2002); *MEHL/Biophile Int'l Corp. v. Milgraum*, 192 F.3d 1362, 1366 (Fed.Cir.1999); *Atlas Powder Co. v. Hanex Prods., Inc.*, 190 F.3d 1342, 1348-49 (Fed. Cir.1999)).

The district court addressed the issue of inherent anticipation in this case, but it found in favor of SmithKline because Apotex did not prove by clear and convincing evidence that it was impossible to make pure PHC anhydrate in the United States before the critical date of the '723 patent. *See SmithKline Beecham Corp.*, 247 F.Supp.2d at 1026 ("[I]t is equally possible, as far as anyone knows, that practicing patent [']196 in non-seeded premises—and goodness knows there were some in the United States as of [the critical] date—would not have produced any hemihydrate."). The district court erred in requiring Apotex to meet this standard

of proof, which is too exacting. Apotex did not need to prove that it was impossible to make PHC anhydrate in the United States that contained no PHC hemihydrate, but merely that "the disclosure [of the prior art] is sufficient to show that the natural result flowing from the operation as taught [in the prior art] would result in" the claimed product. *In re Oelrich*, 666 F.2d 578, 581 (CCPA 1981); *accord MEHL/Biophile Int'l Corp.*, 192 F.3d at 1366; *see also Atlas Powder*, 190 F.3d at 1349-50 (affirming the district court's finding of inherent anticipation despite a finding that the inherent element could be avoided by taking "extraordinary measures" when practicing the prior art). Contrary to this court's precedents, the district court's analysis of inherent anticipation did not consider the teachings of the '196 patent separately from the actual production of PHC hemihydrate. *See Schering Corp.*, 339 F.3d at 1380 ("Anticipation does not require the actual creation or reduction to practice of the prior art subject matter; anticipation requires only an enabling disclosure.") (citing *In re Donohue*, 766 F.2d 531, 533 (Fed.Cir.1985)). Thus, whether it was actually possible to make pure PCH anhydrate before the critical date of the '723 patent is irrelevant. The '196 patent suffices as an anticipatory prior art reference if it discloses in an enabling manner the production of PHC hemihydrate. *See id.* The '196 patent discloses a method of manufacturing PHC anhydrate that naturally results in the production of PHC hemihydrate. Consequently, applying the facts as found by the district court to the correct standard, this court holds that claim 1 of the '723 patent is invalid for anticipation by the '196 patent.

The record shows, and SmithKline admits through its proffered arguments, that producing PHC anhydrate according to the '196 patent inevitably results in the production of at least trace amounts of anticipating PHC hemihydrate. The parties do not dispute that the first known existence of PHC hemihydrate resulted from an attempt to produce PHC anhydrate according to the '196 patent. In December 1984, SmithKline

serendipitously made PHC hemihydrate at its Harlow plant while attempting to manufacture PHC anhydrate according to the '196 patent. As discussed previously, Curzons's discovery of PHC hemihydrate in Worthing also occurred while he was making PHC anhydrate according to the '196 patent. Both of these undisputed events support a finding that practicing the '196 patent naturally results in the production of PHC hemihydrate. The district court also found, and the parties do not dispute, that neither Apotex nor SmithKline can presently produce PHC anhydrate that does not contain at least trace amounts of PHC hemihydrate. *See, e.g., SmithKline Beecham Corp.*, 247 F.Supp.2d at 1044 ("Apotex cannot eliminate *all* crystals of hemihydrate . . . ." (emphasis in original)). In sum, the record shows that the manufacture of PHC anhydrate according to the '196 patent necessarily results in the production of PHC hemihydrate. This fact finds further record support in the holding that Apotex would infringe claim 1 of the '723 patent under the "single crystal" claim construction. *Id.* at 1043.

The district court made these findings, at least in part, because PHC anhydrate produced at the parties' manufacturing facilities would convert to PHC hemihydrate because the facilities had been "seeded" with PHC hemihydrate crystals. *Id.* SmithKline takes the position that Apotex's infringement will result wholly from the PHC hemihydrate "seeds" present in Apotex's facility, and that Apotex could avoid infringement if it manufactured PHC anhydrate in a facility clean of hemihydrate "seeds." While PHC hemihydrate "seeds" will certainly exacerbate the presence of PHC hemihydrate in Apotex's PHC anhydrate pills, this court does not accept SmithKline's assertion that the hemihydrate "seeds" will be the sole cause of the undesired PHC hemihydrate in Apotex's anhydrate pills. Indeed, SmithKline argued at trial that PHC hemihydrate "seeds" are not necessary to produce PHC hemihydrate.

SmithKline's position on the source of Apotex's alleged infringement is inconsistent with the undisputed creation of PHC hemihydrate as discussed *supra*. The production of PHC anhydrate at both SmithKline's Harlow and Worthing plants resulted in the serendipitous production of PHC hemihydrate. The only plausible explanation for this appearance of PHC hemihydrate at the Harlow plant and the likely explanation for its appearance at the Worthing plant is that PHC hemihydrate arises as a natural derivative of practicing the '196 patent. SmithKline did not offer any evidence that pure PHC anhydrate can be produced in facilities that are not seeded. *Id.* at 1035 (district court noting the absence of any experiments by SmithKline to show the difference between PCH anhydrate manufactured in a facility both before and after it is "seeded"). SmithKline's only counter to this explanation is that it had been manufacturing PHC anhydrate according to the '196 patent for years before the hemihydrate was first detected in 1995. SmithKline would have the court infer from this argument that it is possible to make pure PHC anhydrate according to the '196 patent in unseeded conditions. The district court, however, properly dismissed this logic noting that "existence and detection are not the same thing." *Id.* at 1022. The district court went on to explain that PHC hemihydrate may have existed in undetectable amounts since Ferrosan first produced PHC anhydrate in the 1970s, particularly because the technology to detect PCH hemihydrate in small amounts did not exist until 1985. The district court reasoned that it may also be possible for PHC anhydrate to coexist with low levels of PHC hemihydrate without further conversion, thereby rejecting SmithKline's argument that the absence of conversion in early batches of PHC anhydrate prove that the hemihydrate form did not exist prior to 1984. *See id.* at 1022-23 (reconciling conflicting expert testimony by discussing a possible equilibrium point at which conversion plateaus at a few percentage points), 1031 ("[H]emihydrate in small amounts does nothing for the

anhydrate with which it is mixed.") & 1035 (noting that inconsistent test results "impl[y] that the hemihydrate and the anhydrate can coexist in an equilibrium").

Because the record contains clear and convincing evidence that production of PHC anhydrate in accordance with the '196 patent inherently results in at least trace amounts of PHC hemihydrate, this court holds that the '196 patent inherently anticipates claim 1 of the '723 patent under 35 U.S.C. § 102(b). Consequently, it was legal error for the district court to base its finding of no inherent anticipation upon a finding that Apotex did not present clear and convincing evidence that PHC hemihydrate existed before the critical date of the '723 patent. Additionally, the district court's supposition that Apotex could possibly prevent PHC anhydrate from converting to PHC hemihydrate by building a new plant that was not seeded with PHC hemihydrate, or by preventing the PHC anhydrate from being exposed to moisture, does not change this result. This court's law does not require Apotex to take extraordinary measures to practice the prior art without infringing claim 1 of the '723 patent. *See Atlas Powder*, 190 F.3d at 1349-50 (affirming the district court's finding of inherent anticipation despite a finding that the inherent element could be avoided by taking "extraordinary measures" when practicing the prior art).

SmithKline has sued Apotex for infringement of the '723 patent in an express attempt to prevent Apotex from practicing the '196 patent upon its expiration. In *Atlas Powder*, this court noted that one of the principles underlying the doctrine of inherent anticipation is to ensure that "[t]he public remains free to make, use or sell prior art compositions or processes, regardless of whether or not they understand their complete makeup or the underlying scientific principles which allow them to operate." 190 F.3d at 1348; *accord Schering Corp.*, 339 F.3d at 1379-80. Invalidating claim 1 of the '723 patent

for inherent anticipation by the '196 patent furthers this policy of allowing the public to practice expired patents.

This holding is also in accord with this court's precedent. *In re Seaborg*, 51 C.C.P.A. 1109, 328 F.2d 996 (CCPA 1964), held that claims for an isotope of americium made by a nuclear reaction were not inherently anticipated by a prior art patent disclosing a similar nuclear reaction process but with no disclosure of the claimed isotope. In finding no anticipation, this court's predecessor found "no positive evidence" that the claimed isotope was inherently produced by the prior art process. *Id.* at 999. The court properly held that the mere "possibility" that the small amount of the claimed element "may have been produced" was insufficient to invalidate the claim for anticipation. *Id.* Similarly, it is undisputed that SmithKline's and Apotex's practice of the '196 patent results in the production of the claimed PHC hemihydrate in trace amounts.

As noted in *Schering Corp.*, a patentee may obtain patent protection for an inherently anticipated compound through proper claiming. 339 F.3d at 1381. This court's holding today merely precludes patent protection for the bare compound PHC hemihydrate as claimed in claim 1 of the '723 patent because the compound is inherently anticipated by the '196 patent.

Miscellaneous Issues

SmithKline also appealed the district court's decision to prevent SmithKline from pursuing its contributory infringement claim. As discussed above, that claim asserted that the ingestion of Apotex's PHC anhydrate tablet by a patient would result in conversion to PHC hemihydrate. Again, SmithKline's allegations of contributory infringement based upon the theory that PHC anhydrate converts into PHC hemihydrate upon ingestion further supports this court's finding of inherent anticipation. Nevertheless, because claim 1 is inva-

lid for anticipation under § 102(b), SmithKline's appeal on contributory infringement is moot.

Similarly, SmithKline's appeal of the district court's ruling that injunctive relief under 35 U.S.C. § 271(e)(4) is within the district court's discretion is also moot. That ruling was not necessary for the district court's judgment below and is immaterial to the determination of this appeal. This court, therefore, does not address that issue in this opinion.

III.

In summary, this court reverses the claim construction of the district court and holds that claim 1 of the '723 patent covers any amount of crystalline paroxetine hydrochloride hemihydrate without further limitation. Based on the factual findings of the district court, this court affirms the district court's finding that Apotex's PHC anhydrate product will infringe claim 1 under that broad construction. Notwithstanding that conclusion, this court holds, based on the undisputed facts, that claim 1 of the '723 patent is invalid for inherent anticipation by the '196 patent under § 102(a). Apotex is, therefore, not liable for infringing claim 1 of the '723 patent. This court affirms the district court's judgment.

COSTS

Each party shall bear its own costs.

AFFIRMED

GAJARSA, *Circuit Judge*, concurring.

I join in the judgment of the court, however, I reach the judgment by a different road. I would find that the trial court erred in construing Claim 1 of the '723 patent. Under the correct construction, SmithKline Beecham ("SKB") has proven a prima facie case that Apotex's product will infringe Claim 1. Claim 1, however, is invalid because it encompasses subject matter that is unpatentable under 35 U.S.C. § 101.[1] I would affirm the district court's judgment in favor of Apotex on the basis that Claim 1 encompasses unpatentable subject matter pursuant to § 101 contrary to the finding of the majority that claim 1 is invalid pursuant to § 102(b). Although the majority outlines the factual background, I deem it necessary to add more specificity to the historical background.

In the 1970s, scientists at the Danish company of A/S Ferrosan ("Ferrosan") first synthesized a new class of chemical compounds. At least some of these compounds were reported to selectively inhibit the reuptake of serotonin, a naturally occurring chemical in the brain. Several commercial antidepressants common at the time inhibited the neuronal reuptake of serotonin. Ferrosan's laboratory tests indicated that its new compounds inhibited serotonin-uptake in a manner comparable to that exhibited by these existing antidepressant drugs.

Ferrosan applied for, and on February 8, 1977, was assigned, U.S. Patent No. 4,007,196 ("the '196 patent"). Paroxetine was among the compounds that Ferrosan discovered and that the '196 patent protected. In 1980, Ferrosan granted Beecham Group Limited (now part of SKB) an exclu-

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[1] "Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title." 33 U.S.C. § 101.

sive license to make, to have made, to use, and to sell paroxetine throughout the world (save for specified Scandinavian countries).

In 1981, SKB began manufacturing paroxetine hydrochloride in its Harlow (U.K.) plant. These early manufacturing activities did not lead to a commercial product immediately. Before a new pharmaceutical drug can be placed on the U.S. market, it must undergo elaborate testing for safety and efficacy. Quantities of paroxetine hydrochloride were distributed to different parts of the world, including the U.S., for use in clinical trials. SKB scientists also experimented with paroxetine hydrochloride in its bulk form (i.e., its form prior to being made into pills) to improve the production of the bulk material.

SKB's experimentation on bulk form paroxetine led to an important discovery. On May 29, 1985, an SKB scientist named Alan Curzons issued a memorandum entitled "Paroxetine Polymorphism." In the memorandum, Curzons stated that paroxetine "had been shown to exist in two discreet [sic] crystalline polymorphic FORMS," a stable, nonhygroscopic hemihydrate and a hygroscopic anhydrate. Curzons's tests confirmed that the anhydrate and the hemihydrate were indeed distinct crystalline forms of paroxetine.

Crystallinity is central to understanding both Curzons's reference to polymorphism and this case. "Polymorphs" are distinct crystalline structures containing the same molecules. These structural differences can affect various properties of the crystals, such as melting points and hardness (e.g., graphite and diamonds are both crystalline forms of carbon). The two forms of paroxetine hydrochloride that Curzons discovered were technically "pseudopolymorphs," though pseudopolymorphs are often loosely called polymorphs (an apparently common looseness that the district court adopted and that I have retained in this opinion). Pseudopolymorphs not only have their molecules arranged differently but also have a

slightly different molecular composition. A common type of pseudopolymorph is a *solvate*, which is a crystal in which the molecules defining the crystal structure "trap" molecules of a solvent. The crystal molecules and the solvent molecules then bond to form an altered crystalline structure. When the trapped and bonded solvent is water, the solvate is called a *hydrate*. Hydrates bonding one water molecule to every two of the other molecules constituting the unit crystal cell are called *hemihydrates*. Paroxetine hydrochloride hemihydrate ("paroxetine hemihydrate") is a crystalline structure binding one water molecule to every two paroxetine hydrochloride molecules. Despite the presence of water molecules, a hemihydrate is a solid, a powder, at room temperature.

Prior to Curzons's discovery, the only known form of paroxetine hydrochloride had been an anhydrate, a crystalline form of paroxetine that does not contain a bound water molecule. In May 1985, Curzons made a batch of paroxetine, added isopropyl alcohol, a solvent, and found that the batch crystallized as a hemihydrate rather than as an anhydrate. Curzons immediately recognized the significance of the hemihydrate—its superior handling properties—as well as its potential for a new patent relating to those properties.

These superior handling properties are natural effects of water bonded into the paroxetine hemihydrate. The anhydrous form of crystalline paroxetine hydrochloride ("paroxetine anhydrate") is hygroscopic; that is, it attracts water. This water is not attached to the paroxetine anhydrate by molecular bonds. As a result, the water is easily dispersed by heating paroxetine anhydrate at a significantly lower temperature than would be required to liberate the water molecule bound in paroxetine hemihydrate crystals. The anhydrate's hygroscopicity makes it difficult to handle in the manufacturing process; measures must be taken to control humidity and other sources of moisture, lest "soggy" anhydrate degrade into other compounds in ways that might impair the safety or

the efficacy of the product. Because the hemihydrate is not hygroscopic, it is easier to handle with fewer precautionary measures protecting its safety and efficacy.

Beecham applied for a British patent on Curzons's discovery on October 25, 1985, and for a U.S. patent on October 23, 1986. On January 26, 1988, the U.S. Patent and Trademark Office (PTO) issued the '723 patent, entitled "Anti-depressant Crystalline Paroxetine Hydrochloride Hemihydrate," which, according to the Abstract, "provides crystalline paroxetine hydrochloride hemihydrate, processes for its preparation, compositions containing the same and its therapeutic use as an anti-depressant." '723 patent.

The claims as issued were identical to those in the original application. The '723 patent combines product claims (Claims 1, 2, 3, and 5), process claims (Claim 4), and use claims (Claims 5 and 6). Only Claim 1 is at issue in the current litigation. It reads:

1. Crystalline paroxetine hydrochloride hemihydrate.

Subsequent experimentation taught SKB a few additional lessons about paroxetine hemihydrate. First, SKB learned that hemihydrate likely existed at least as early as December 1984 (and possibly earlier), even though Curzons did not identify it as such until 1985. Second, and more significantly, SKB learned that the two forms of paroxetine are related through a phenomenon known as "disappearing polymorphs."[2] At times, the appearance of a new polymorph (or pseudopolymorph)—hemihydrate—may affect the process that was previously used to make the old polymorph—anhydrate. The result is such that the same process will no

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[2] Dr. Joel Bernstein, one of SmithKline's expert witnesses at the trial, is an authority on "disappearing polymorphs." *See* Joel Bernstein, *Polymorphism in Molecular Crystals* 89-92 (2002); J.D. Dunitz & J. Bernstein, "Disappearing Polymorphs," 28 *Accounts of Chem. Res.* 193 (1995).

longer produce the old polymorph—at least (as here) in its pure form.

The causal mechanism of polymorphic creation and transformation is not clear. Modern science does not yet understand the full complexity of the atomic interactions at play in the phenomenon of polymorphism, and specifically in the disappearance of some polymorphs. Scientists have, however, identified three factors believed to be significant. First, later-appearing polymorphs tend to be more stable than earlier ones. Because a stable crystalline form is not as likely to change into a less stable one than vice versa, there tends to be a "natural" drift toward more stable polymorphs. Second, impurities retard crystallization, including crystallization into new forms. Technological progress in manufacturing—including chemical manufacturing—has allowed manufacturers to reduce the impurities in their products. Because of this increased purity technology creates increasingly favorable conditions for the "natural" drift towards stability. Third, and most significantly to this case, once a new and more stable crystal emerges, should it be mixed, even in very small quantities, with the old, less stable crystal, the old form may convert to the new.

This process of "seeding" a batch of the old crystalline structure with its new, stable polymorphs can serve as a method of manufacturing the new polymorph by "converting" the old into the new. Seeding and conversion can also be accidental side-effects of new, stable crystals becoming airborne and "contaminating" the laboratory or plant in which the old crystal is being manufactured. While controlled conversions in the former case are obviously desirable production methods, natural conversion in the latter case may be undesirable interferences with the production of the old polymorph.

Seeding and conversion are central to this case. A single crystal of paroxetine hemihydrate can seed an environment to induce conversion—and to render the production of pure

paroxetine anhydrate in that environment impossible. While it is often possible, at least in theory, to build clean unseeded environments in which the old process will produce pure forms of the original polymorph, that possibility often remains only a matter of theory; seeds introduced into the environment frequently permeate all parts of the globe and render it impossible to develop such clean environments. No one knows whether it is possible today to build clean environments in which a pharmaceutical company could produce pure paroxetine anhydrate. Nor, for that matter, is anyone certain precisely what caused the first crystal of paroxetine hemihydrate to form—though it does appear likely that a crystal from that December 1984 batch of paroxetine hemihydrate seeded Curzons's laboratory prior to his initial identification of the paroxetine hemihydrate polymorph.

As noted, scientific uncertainty surrounds the entire phenomenon of disappearing polymorphs, as well as its particular manifestation in paroxetine. Apotex's expert,[3] in fact, testified that the phenomenon does not manifest itself in paroxetine, and that paroxetine anhydrate and paroxetine hemihydrate can coexist happily in a single batch of paroxetine.

After weighing the testimony of all of the experts, the district court hypothesized that while the presence of paroxetine hemihydrate seeds in a batch of paroxetine anhydrate is likely, only a small percentage of the paroxetine anhydrate is likely to convert to hemihydrate under normal conditions of humidity, temperature, or pressure. The district court continued to hypothesize that given enough humidity, heat, or pressure, conversion may continue until it reaches 100 percent, and that by the same token, with much tighter controls less, maybe no, conversion will take place despite the presence of seeds. Finally, the district court noted that the

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[3] Dr. Terence Threlfall

clearest case of limited conversion occurs where there are no water molecules in the environment of the anhydrate.

For the purposes of this case, the district court admitted all proffered expert testimony concerning both disappearing polymorphism as a scientific phenomenon and its applicability to paroxetine, and found it to be a credible explanation of various factual occurrences in the discovery and the spread of paroxetine hemihydrate.

This language is all straightforward, and Claim 1—containing only four words—is the most straightforward of all. The plain language of a claim asserting rights to "crystalline paroxetine hydrochloride hemihydrate" claims any amount of "crystalline paroxetine hydrochloride hemihydrate." The plain language of this claim is precisely the "single crystal" theory that the district court rejected on other grounds. The district court explicitly recognized that the claim's plain language included even a single crystal of hemihydrate; the district court rejected that construction on the grounds that it would have "absurd consequences."

The district court suggested that even SKB had expressed some discomfort with the implications of the "single crystal" construction of Claim 1. As a result, throughout the course of this litigation, both parties and two trial judges have considered multiple limitations that could be read into the claim—each of which proposed a minimum amount considerably larger than a single crystal. During the summary judgment hearing, Judge Kocoras dismissed several attempts to introduce such limitations. Though he himself never adopted a construction, his ruling that SKB could admit evidence of infringement developed using all available testing techniques implies that SKB could pursue an infringement claim against anyone making, using, or selling detectable amounts of paroxetine hemihydrate. In his ruling following the bench trial, Judge Posner noted that under "ordinary" circumstances, claims with unambiguous plain language

should be interpreted in a manner consistent with that plain language. There is little doubt that the "single crystal" interpretation is the only one consistent with the claim's plain language.

Nevertheless, many of the "absurd consequences" that that the district court foresaw are, in fact, absurd, and would ill-serve the public were they the law. The proper place for resolutions of such conflicts between patent law and patent policy, however, is Congress, not the courts. For the most part, though, such absurdities are likely to lie not in the law itself, but rather in misapplications of the law. Here, the district court applied two additional elements of patent law to avoid the perceived absurdities. The district court found the single crystal theory indefinite, and applied various rules of claim construction to save the claim by limiting its scope. The district court introduced a limitation explicitly excluding hemihydrate produced by involuntary conversion of a proportion of an anhydrous mixture so small as to lack any commercial significance.

This conclusion, however, misinterprets the meaning of indefiniteness. The district court was certainly correct that indefinite claims could create socially undesirable "zone[s] of uncertainty which enterprise and experimentation may enter only at the risk of infringement claims." *United Carbon Co. v. Binney & Smith Co.*, 317 U.S. 228, 236, 63 S.Ct. 165, 87 L.Ed. 232 (1942). Such zones would undoubtedly "discourage invention only a little less than [would] unequivocal foreclosure of the field." *Id.* The district court nevertheless erred in concluding that the mere possibility that a single crystal interpretation might discourage innovation and experimentation necessarily rendered the claim indefinite. The proper standard for assessing whether a patent claim satisfies the statutory requirement of definiteness is whether one skilled in the art would understand the bounds of the claim when read in light of the specification. *Miles Labs., Inc. v.*

Shandon, Inc., 997 F.2d 870, 875 (Fed.Cir.1993); *Exxon*, 265 F.3d 1371, 1375 (Fed.Cir.2001).

As the Supreme Court has noted, all patents are capable of discouraging at least some innovation. *Brenner v. Manson*, 383 U.S. 519, 534, 86 S.Ct. 1033, 16 L.Ed.2d 69 (1966) ("[H]ow likely is disclosure of a patented process to spur research by others into the uses to which the product may be placed? To the extent that the patentee has power to enforce his patent, there is little incentive for others to undertake a search for uses."). This discouragement, however, is simply part of the cost that the public bears to promote an overall patent system whose goal is to motivate more innovation than it deters. It is certainly possible that some individual patents will not have the desired effect, and will deter more innovation than they motivate. While such a result would hardly serve the public interest, this negative policy outcome is insufficient alone to render a patent claim indefinite. Indefiniteness must be examined within the framework provided by statute as clarified by our case law. We recently explained that "[a] claim is indefinite if, when read in light of the specification, it does not reasonably apprise those skilled in the art of the scope of the invention." *Amgen Inc. v. Hoechst Marion Roussel*, 314 F.3d 1313, 1342 (Fed.Cir.2003). The contrapositive of this statement is also true. If the claim, read in light of the specification, reasonably apprises those skilled in the art of the scope of the invention, it is definite within the meaning of 35 U.S.C. § 112(2).

Given that standard, the district court's error is evident. The plain language of Claim 1 is unambiguous. It claims "crystalline paroxetine hydrochloride hemihydrate," unambiguously meaning *all* "crystalline paroxetine hydrochloride hemihydrate," without any exceptions. Nothing in the claim language contradicts this straightforward interpretation—nor, for that matter, does anything in the patent's written description, the patent's figures, or the prosecution history. There is

no reason for anyone, much less one skilled in the art, to read this plain language as meaning anything else, nor to believe that the patent meant to exclude small or trace amounts of crystalline paroxetine hydrochloride hemihydrate from its coverage. Those skilled in the art should certainly have appreciated the scope of the invention—even if they also viewed its breadth as damaging to their own efforts in experimentation and invention.

The district court read limitations from the written description into the claim language for reasons that appear to have stemmed from its public policy concerns. The court's motivation notwithstanding, the practice of reading limitation from written descriptions into claims invariably leads to misconstrued claims. Simply pointing to discussions in the specification or prosecution history cannot rebut the presumption that claims should be afforded their ordinary meanings. *CCS Fitness, Inc. v. Brunswick Corp.*, 288 F.3d 1359, 1366 (Fed.Cir.2002). "We recognize that there is sometimes a fine line between reading a claim in light of the specification, and reading a limitation into the claim from the specification." *Comark Communications v. Harris Corp.*, 156 F.3d 1182, 1187 (Fed.Cir.1998) (citations omitted). In this case, there is little doubt that the district court crossed that line.

The "single crystal" theory provides the only interpretation that is entirely consistent with the language of Claim 1 of the '723 patent. This interpretation meets the statutory requirement for definiteness. It puts those skilled in the art on notice that the '723 patent protects crystalline paroxetine hydrochloride hemihydrate, in all amounts, and that any manufacture, use, or sale of this compound—including inadvertent manufacture, use, or sale—would infringe the '723 patent. The correct construction of Claim 1 adheres to the single crystal theory.

Because the '723 patent claims every single crystal of paroxetine hemihydrate, and because Apotex's paroxetine product contains at least some hemihydrate crystals, SKB has proven that Apotex's product prima facie infringes—if Claim 1 is valid. Because Claim 1 is broad enough to encompass both patentable and unpatentable subject matter, however, I would find that it is invalid under 35 U.S.C. § 101.

I.

Authority

The question of patentability under section 101 does not arise often, and a court's decision to raise it sua sponte is even less common. The centrality of patentable subject matter to the entire scope of the patent law suggests that there are times when such inquiries are critical. The Supreme Court established long ago that "the question whether the invention, which is the subject-matter in controversy, is patentable or not is always open to the consideration of the court, whether the point is raised by the answer or not." *Slawson v. Grand St. R.R.*, 107 U.S. 649, 652, 2 S.Ct. 663, 27 L.Ed. 576 (1882). *See also Richards v. Chase Elevator Co.*, 158 U.S. 299, 301, 15 S.Ct. 831, 39 L.Ed. 991 (1895). These precedents remain good law, though the courts have relied upon them infrequently. The policy that drove them, however, remains vibrant. Less than a decade after *Slawson*, in the context of an interference, the Supreme Court stressed that

> [t]he parties to the present suit appear to have been willing to ignore the question as to patentability in the present case, and to have litigated merely the question of priority of invention, on the assumption that the invention was patentable. But neither the Circuit Court nor this court can overlook the question of patentability.

Hill v. Wooster, 132 U.S. 693, 698, 10 S.Ct. 228, 33 L.Ed. 502 (1890). In our law, 37 C.F.R. § 41.77(b) specifically

allows an administrative patent judge to raise the issue of patentability sua sponte as to claims designated to correspond to a count of an interference.

Beyond administrative proceedings, courts have found the occasional need to raise section 101 issues sua sponte—even subsequent to the 1952 revisions to the Patent Act. At least three of our sister circuits, whose rulings on patent law prior to 1982 do not bind this court but retain persuasive value, raised section 101 issues that the parties had not addressed. The Ninth Circuit announced that "it is the duty of the court to dismiss a patent infringement suit whenever it affirmatively appears that the patent is invalid." *Barkeij v. Lockheed Aircraft Corp.*, 210 F.2d 1, 2 (9th Cir.1954). According to the Second Circuit, "[e]ven were section 101 not raised by appellees, it was not error for the district court to consider it since it had the power to do so. Section 101 deals with the subject matter of patents and, as such, it is always open to the consideration of the court . . . ." *Howes v. Great Lakes Press Corp.*, 679 F.2d 1023, 1028 (2d Cir.1982). And the Third Circuit explained that

> [i]t has been clear from an early date, that the court could dismiss a bill because the invention described in the patent was not patentable, even when no defense of invalidity was set up in the answer. . . . Accordingly, when a party brings suit on a patent alleging infringement, it is accountable for the validity of the patent . . . .

Borden Co. v. Clearfield Cheese Co., 369 F.2d 96, 99-100 (3d Cir.1966).

The Federal Circuit has independently raised section 101 concerns without prompting from the parties at least once before. In *Titanium Metals Corp. v. Banner*, 778 F.2d 775 (Fed.Cir.1985), we considered a patent that the PTO had rejected as both anticipated under Section 102 and obvious

under Section 103. *Id.* at 776. The district court reversed, and issued an order authorizing the Commissioner of Patents and Trademarks to issue the patent. *Titanium Metals Corp. v. Mossinghoff*, 603 F.Supp. 87, 91 (D.D.C.1984). The government appealed. The matter therefore reached this court on issues relevant to sections 102 and 103, not to section 101. We explained, however, that

> [t]he patent law imposes certain fundamental conditions for patentability, paramount among them being the condition that what is sought to be patented, as determined by the claims, be new. The basic provision of Title 35 applicable here is § 101 . . . . The title of the application here involved is "Titanium Alloy," a composition of matter. Surprisingly, in all of the evidence, nobody discussed the key issue of whether the alloy was new, which is the essence of the anticipation issue . . . .

Titanium Metals, 778 F.2d at 781. We concluded that "the decision and order of the district court holding that claims 1, 2, and 3 are directed to patentable subject matter and authorizing the issuance of a patent thereon were clearly erroneous and are reversed." *Id.* at 783. In other words, we recognized that we could neither affirm nor reverse the district court's holdings under Sections 102 and 103 in a principled way without addressing the underlying erroneous assumption that the invention at issue met the requirements of section 101. *See also Brassica Prot. Prods. LLC v. Sunrise Farms (In re Cruciferous Sprout Litig.)*, 301 F.3d 1343, 1350 (Fed.Cir. 2002) (characterizing as "common sense" *Titanium Metals*' rationale, including the injection of section 101 into an anticipation analysis).

Both this court and the Supreme Court have recognized that there is a significant public policy interest in removing invalid patents from the public arena. In *Cardinal Chem. Co. v. Morton Int'l, Inc.*, 508 U.S. 83, 100, 113 S.Ct. 1967, 124 L.Ed.2d 1 (1993), the Supreme Court reversed our practice of

vacating findings of invalidity where the court found non-infringement in light of the strong public interest in resolving questions of patent validity. In *Blonder-Tongue Labs., Inc. v. Univ. of Ill. Found.*, 402 U.S. 313, 91 S.Ct. 1434, 28 L.Ed.2d 788 (1971), the Supreme Court commented at length on the wasteful consequences of relitigating the validity of a patent after it has once been held invalid. In *United States v. Glaxo Group, Ltd.*, 410 U.S. 52, 57-58, 93 S.Ct. 861, 35 L.Ed.2d 104 (1973), the Supreme Court ruled that the government, like patent licensees, could always challenge the validity of a patent in the course of prosecuting an antitrust action "to vindicate the public interest in enjoining violations of the Sherman Act." The Court cited numerous cases[4] as "sufficient authority" to support this holding, *id.*, which it saw as furthering a longstanding policy: "It is as important to the public that competition should not be repressed by worthless patents, as that the patentee of a really valuable invention should be protected in his monopoly. . . ." *Pope Mfg. Co. v. Gormully*, 144 U.S. 224, 234, 12 S.Ct. 632, 36 L.Ed. 414 (1892).

These decisions mirror our own recognition that "[p]ublic policy requires that only inventions which fully meet the statutory standards are entitled to patents." *Constant v. Advanced Micro-Devices, Inc.*, 848 F.2d 1560, 1564 (Fed.Cir. 1988) (citations omitted), and that "[t]here is a stronger public interest in the elimination of invalid patents than in the affirmation of a patent as valid." *Nestier Corp. v. Menasha*

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[4] *Telephone Cases*, 167 U.S. 224, 17 S.Ct. 809, 42 L.Ed. 144 (1897); *United States v. United States Gypsum Co.*, 333 U.S. 364, 68 S.Ct. 525, 92 L.Ed. 746 (1948); *Sola Elec. Co. v. Jefferson Elec. Co.*, 317 U.S. 173, 63 S.Ct. 172, 87 L.Ed. 165 (1942); *Edward Katzinger Co. v. Chicago Metallic Mfg. Co.*, 329 U.S. 394, 67 S.Ct. 416, 91 L.Ed. 374 (1947); *MacGregor v. Westinghouse Elec. & Mfg. Co.*, 329 U.S. 402, 67 S.Ct. 424, 91 L.Ed. 380 (1947); *Pope Mfg. Co. v. Gormully*, 144 U.S. 224, 234, 12 S.Ct. 632, 36 L.Ed. 414 (1892); and *Lear, Inc. v. Adkins*, 395 U.S. 653, 670, 89 S.Ct. 1902, 23 L.Ed.2d 610 (1969).

Corp.-Lewisystems Div., 739 F.2d 1576, 1581 (Fed.Cir.1984). The best way to ensure that patents issue only for inventions in full compliance with the statutory standards is to allow "the validity of a patent, which was originally obtained in ex parte proceedings in the PTO, [to] be challenged in court." *Constant*, 848 F.2d at 1564.

The sua sponte section 101 inquiry that this case warrants therefore falls well within a long if somewhat sparse tradition, driven in part by concerns of public policy but grounded entirely in legal authority. Where, as here, the facts are both unusual[5] and undisputed, where the legal implication of these facts is clear, and where a consideration of fundamental aspects of law and policy is necessary to maintain the integrity of the patent law, a sua sponte inquiry into the patentability of the claimed subject matter is appropriate.

II.

Theory of Infringement

Because the proper construction of Claim 1 follows the "single crystal" theory, SKB must prove that Apotex's product does and will continue to contain at least some hemihydrate. Though SKB's legal burden is only to prove infringement by a preponderance of the evidence, *S. Bravo Sys.*,

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[5] The district court's maze of alternative claim constructions and theories finding Apotex not liable for infringement, plus the theory added by the majority, attest to the unique circumstances of this case. The district court's opinion, and in particular its attempt to introduce a novel equitable defense, *SmithKline Beecham Corp. v. Apotex Corp.*, 247 F.Supp.2d 1011, 1043-45 (N.D.Ill.2003) ("*SK II*"), strongly imply that something "feels wrong" about holding an infringer liable for inevitable, spontaneous infringement. We therefore face a choice. We can either address the issue head-on and explain why an attempt to patent unpatentable subject matter leads to so many apparent anomalies, or we can try to contort the aspects of patent law raised by the parties in order to avoid those anomalies. I believe that the law is best served by adopting the straightforward approach.

Inc. v. Containment Techs. Corp., 96 F.3d 1372, 1376 (Fed.Cir.1996), SKB nevertheless faces a significant challenge. As the district court found, Apotex wants to manufacture pure anhydrate; any hemihydrate present in its product is an undesirable impurity. *See SK II*, 247 F.Supp.2d at 1015, 1025 & 1045. Both SKB and the district court explicitly rejected the possibility that the anhydrous and hemihydrous forms of paroxetine came into existence simultaneously, and that every batch of paroxetine ever manufactured (or that ever will be manufactured) contains at least trace elements of hemihydrate—an argument that would not only prove SKB's point about Apotex's product, but would also invalidate the '723 patent as inherent in the prior art. *Id.* at 1025.

SKB's basic theory of infringement, which the district court recognized as establishing a prima facie case of infringement when applied to the single crystal construction, *id.* at 1043, rests upon two scientific principles that remain matters of controversy within the scientific community, both as a general phenomena and as applied to paroxetine: seeding and conversion. *See id.* at 1021-23. Under this infringement theory, the form of paroxetine discovered in the 1970s was, indeed, pure anhydrate; hemihydrate did not exist until late 1984.

> [SKB's expert] Dr. Bernstein testified that he was 'absolutely convinced' that no hemihydrate had existed before December 1984 . . . Dr. Terence Threlfall, Apotex's expert on polymorphism, testified [that] Dr. Bernstein's absolute certainty . . . is not tenable. No one knows when the hemihydrate form of paroxetine came into existence, although it is a reasonable inference that it did not exist in a detectable amount until then.

Id. at 1022. From that date forward, however, it was impossible to produce pure anhydrate in a "seeded" environment because even under normal climactic conditions, at

least some of the anhydrate would "convert" to become hemihydrate.

> This process of 'seeding' the old with the new can be deliberate—that is, can be a method of manufacturing the new polymorph—or adventitious, a result of the fact that some of the crystals become airborne and 'contaminate' the laboratory or plant in which the old crystal is being manufactured . . . . [T]he seeds relevant to this case are seeds that cause one polymorph to convert to another and these seeds are crystals of the form to which conversion occurs. A single tiny crystal, constituting a single seed, might induce conversion . . . . The creation of the new polymorph is likely to make the laboratory or plant where it is produced seeded, with the result that efforts to produce the old polymorph may instead produce the new one, since it is the more stable form. In principle it should be possible to re-create the old polymorph, just by replicating the exact procedure by which it used to be created, only this time in a seed-free environment . . . . [I]n practice efforts to re-create old polymorphs do not always succeed, probably because the critical mass of molecules that is required to cause conversion is so minute . . . .

Id. at 1020. SKB therefore argues that any paroxetine manufactured in a seeded environment must inevitably contain at least some hemihydrate, that this condition has only prevailed since some time in late 1984, and that Apotex's facilities have been or inevitably will become seeded.

> According to SmithKline, the BCI plant [in which Apotex manufactures anhydrate] is seeded with hemihydrate crystals because it was there that Apotex, exercising the broadened experimental-use privilege conferred by the Hatch-Waxman Act, used and made hemihydrate in the course of developing its anhydrous product.

Id. at 1024.

III.

SKB's proof supporting this theory must rest upon factual demonstrations. As an appellate court, we accept all facts found by the district court unless they are clearly erroneous. *Shockley v. Arcan, Inc.*, 248 F.3d 1349, 1357 (Fed.Cir.2001). The district court, however, stated its most significant finding as an hypothesis:

> The conflicting testimony of Bernstein . . . on the one hand and of Threlfall on the other can largely be reconciled on the following hypothesis: while the presence of hemihydrate seeds in a batch of anhydrate is likely, provided the ambient humidity and temperature are no lower than is normal in the temperate zone, to produce conversion within a short time, once the amount converted reaches a few percent of the mixture further conversion is unlikely without substantially greater humidity, temperature, or pressure.

SK II, 247 F.Supp.2d at 1022-23. Findings of fact stated as hypotheses pose particularly challenging problems for appellate courts. Did the district court accept this hypothesis as a fact upon which legal arguments and conclusions can rest, or was the district court merely trying to make sense of the scientific testimony that the two experts proffered?

The district court's own legal conclusions make it clear that the court accepted them as facts, by stating, for example, that "[Apotex's] BCI plant *is* seeded as a result of the mid-1990s experiments," *id.* at 1032 (emphasis added), and that "the anhydrate as it proceeds through the process [at the BCI plant] will at several junctures be exposed to air that contains enough water molecules to permit conversion of anhydrate to hemihydrate." *Id.* These statements make sense *only* if the district court found that both seeding and conversion are valid scientific facts, at least as applied to paroxetine for the purposes of this case.

The district court's understandable hedging of its language when dealing with controversial scientific theories nevertheless led it to definitive factual conclusions: "BCI *probably* will be 'making' at least some hemihydrate crystals and therefore infringing, at least prima facie, patent 723 if claim 1 is interpreted to cover single crystals of the hemihydrate." *Id.* (emphasis added). "Some conversion from anhydrate to hemihydrate *is likely* to occur in a seeded facility in which the anhydrate is exposed to air; BCI's plant is seeded; and the anhydrate manufactured there is exposed to nondehumidified air before it leaves the plant." *Id.* (emphasis added). But in concrete syllogistic conclusion, "[t]his evidence *is sufficient to support an inference* that BCI will be making at least tiny amounts of the hemihydrate if it is permitted to manufacture the anhydrate." *Id.* (emphasis added).

The district court therefore found, as a matter of fact, that paroxetine anhydrate in a seeded environment characterized by normal climactic conditions *can* convert itself spontaneously into paroxetine hemihydrate. *Id.* The district court further found that SKB had met its burden of proving, by a preponderance of the evidence, that such conversion *was inevitable* at Apotex's BCI manufacturing facility. *Id.* at 1042-43.

The district court next turned to consider Apotex's defenses. "If . . . claim 1 is valid and will be infringed . . . by a single crystal of hemihydrate . . . [then] Apotex has a complete affirmative defense that SmithKline is the cause of the infringement." *Id.* at 1052. This conclusion makes sense only after a factual finding that Apotex's legal experimentation with Paxil [6] seeded the BCI plant. *Id.* at 1024. "Apotex

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[6] Under the Hatch-Waxman Act, a generic drug manufacturer is allowed to experiment with a patented drug to prove that its planned product is bioequivalent to one already approved by the Food and Drug Administration (FDA). The district court viewed this statutory permission

cannot eliminate *all* crystals of hemihydrate; under a single-crystal interpretation of claim 1, [and] SmithKline is the sole cause of infringement." *Id.* at 1044 (emphasis in the original).

Finally, the district court explained that

> it is difficult, and in some cases it may be impossible (paroxetine hydrochloride hemihydrate may be one of those cases—no one knows), to destroy all the seeds in seeded premises . . . . Dr. Bernstein testified that if Apotex, desperate to avoid a charge of infringement built a new plant in Antarctica where no hemihydrate seeds had ever been and started manufacturing anhydrate there, and a depressed worker in the plant dropped a Paxil on the floor, the result might be to seed the plant and make it impossible from then on to produce pure anhydrate there.

Id. at 1020-21.

In short, the district court made four critical factual findings: (1) Hemihydrate crystals did not exist before their first emergence in an SKB laboratory in late 1984, *id.* at 1025; (2) Hemihydrate seeds spread easily, and increasingly large parts of the environment are becoming seeded, *id.* at 1020-21; (3) Under normal climactic conditions in a seeded environment, at least some anhydrate crystals will convert spontaneously to become hemihydrate crystals, *id.* at 1022-23; and (4) Apotex's manufacturing facilities have been seeded, *id.* at 1024.

IV.

These findings of fact highlight the unique challenge that the infringement analysis of the '723 patent poses: infringing matter has an unusual tendency to "appear" even where it is

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as an implied license, *SK II*, 247 F.Supp.2d at 1018, and attributed liability for the consequent seeding to SKB. *Id.* at 1044.

unwanted. Such a spontaneous appearance of a patented product vitiates the public notice function of patents. *See id.* at 1028. Under normal circumstances,

> one of ordinary skill in the art should be able to read a patent, to discern which matter is disclosed and discussed in the written description, and to recognize which matter has been claimed. The ability to discern both what has been disclosed and what has been claimed is the essence of public notice. It tells the public which products or processes would infringe the patent and which would not.

PSC Computer Prods. v. Foxconn Int'l, 355 F.3d 1353, 1359 (Fed.Cir.2004). When the claimed product can be "made" via the spontaneous conversion of a noninfringing product into an infringing one, adequate notice is impossible—even if the claimed product was initially synthesized in a laboratory.

Long before 1952, when Section 112 formalized the modern written description requirement, the Supreme Court observed that:

> Whoever discovers that a certain useful result will be produced, in any art, machine, manufacture, or composition of matter, by the use of certain means, is entitled to a patent for it; provided he specifies the means he uses in a manner so full and exact, that any one skilled in the science to which it appertains, can, by using the means he specifies, without any addition to, or subtraction from them, produce precisely the result he describes. And if this cannot be done by the means he describes, the patent is void. And if it can be done, then the patent confers on him the exclusive right to use the means he specifies to produce the result or effect he describes, and nothing more.

O'Reilly v. Morse, 15 How. 62, 119, 14 L.Ed. 601 (1853). The Supreme Court further explained that

> [a]ccurate description of the invention is required by law, for several important purposes: 1. That the government may know what is granted, and what will become public property when the term of the monopoly expires. 2. That licensed persons desiring to practise the invention may know during the term how to make, construct, and use the invention. 3. That other inventors may know what part of the field of invention is unoccupied.

Bates v. Coe, 98 U.S. 31, 39, 25 L.Ed. 68 (1878). While these pre-1952 cases may not apply directly to the modern written description requirement of Section 112, they do demonstrate the longstanding centrality of the public notice function to patent policy.

Paroxetine hemihydrate forces us, for the first time, to confront the requirement that "a patentee specify in a manner so full and exact, that any one skilled in the science to which it appertains, can, by [*avoiding*] the means he specifies," *O'Reilly*, 15 How. at 119, 14 L.Ed. 601, *avoid producing the claimed product*. Otherwise, there will be no way for "other inventors [to] know what part of the field of invention is unoccupied." *Bates*, 98 U.S. at 39. Effective notice is impossible if a natural physical process can convert a non-infringing product into an infringing one.

The district court was correct in concluding that Claim 1 of the '723 patent, subject to the proper single crystal construction, fails to provide suitable notice. *SK II*, 247 F.Supp.2d at 1028, 1052. A paroxetine anhydrate manufacturer, such as Apotex, could exert reasonable efforts to manufacture only products already in the public domain, could direct its entire production process toward developing only products that scrupulously respected all patent rights, and could nevertheless infringe because a natural physical process acting upon

its legitimate anhydrous product "made" new hemihydrous crystals that Apotex then "sold" to the public. "Apotex has tried to prevent conversion of its product to the patented form and a principal issue in this case is whether it has succeeded; there is no suggestion that Apotex *desires* conversion." *SK II*, 247 F.Supp.2d at 1015 (emphasis in original).

Claim 1 therefore cannot be valid. But the failure of notice is a consequence of its invalidity, not the source of it. We must consider whether or not the '723 patent covers only patentable subject matter. *See Slawson*, 107 U.S. at 652.

V.

Patentable Subject Matter

"Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent thereof . . . ." 35 U.S.C. § 101. The Supreme Court has interpreted this statutory range of patentable subject matter to be quite broad, but hardly universal. "In choosing such expansive terms as 'manufacture' and 'composition of matter,' modified by the comprehensive 'any,' Congress plainly contemplated that the patent laws would be given wide scope." *Diamond v. Chakrabarty*, 447 U.S. 303, 308, 100 S.Ct. 2204, 65 L.Ed.2d 144 (1980). That wide scope nevertheless excludes laws of nature, natural phenomena, and abstract ideas. "Such discoveries are 'manifestations of . . . nature, free to all men and reserved exclusively to none.'" *Id.* at 309, 100 S.Ct. 2204, (quoting *Funk Bros. Seed Co. v. Kalo Inoculant Co.*, 333 U.S. 127, 130, 68 S.Ct. 440, 92 L.Ed. 588 (1948)). *See also Diamond v. Diehr*, 450 U.S. 175, 185, 101 S.Ct. 1048, 67 L.Ed.2d 155 (1981); *Parker v. Flook*, 437 U.S. 584, 589, 98 S.Ct. 2522, 57 L.Ed.2d 451 (1978).

"Phenomena of nature, though just discovered, mental processes, and abstract intellectual concepts are not patentable, as they are the basic tools of scientific and tech-

nological work." *Gottschalk v. Benson*, 409 U.S. 63, 67, 93 S.Ct. 253, 34 L.Ed.2d 273 (1972). A single standard applies to product claims and process claims alike. *Id.* "[W]hether patents are allowable for [challenged subject matter] is not a matter of discretion, but of law. . . . Either the subject matter falls within Section 101 or it does not." *Animal Legal Def. Fund v. Quigg*, 932 F.2d 920, 929-30 (Fed.Cir.1991). And as a matter of law, the critical distinction guiding all section 101 inquiries into the patentability of subject matter is that human-made, or synthetic, products or processes are patentable, while products and processes of nature are not. *See Chakrabarty*, 447 U.S. at 313, 100 S.Ct. 2204; *J.E.M. AG Supply v. Pioneer Hi-Bred Int'l*, 534 U.S. 124, 130, 122 S.Ct. 593, 151 L.Ed.2d 508 (2001).

The district court found as a matter of fact that at some point, likely in late 1984, something occurred in SKB's laboratories that gave rise to two new phenomena simultaneously. *SK II*, 247 F.Supp.2d at 1021-22. The first was a synthetic crystal later named paroxetine hemihydrate, *id.*, ostensibly a patentable human-made invention under *Chakrabarty*. The second was a natural physical process whereby paroxetine anhydrate (a pre-existing synthetic crystal that today is in the public domain) could, under normal climactic conditions and with no human intervention, bond with water molecules and convert itself into paroxetine hemihydrate, *SK II*, 247 F.Supp.2d at 1021-22, ostensibly an unpatentable, newly discovered natural process under *Chakrabarty*.

This distinction between the synthetic product and its natural "reproduction" process is subtle, but critical. Paroxetine hemihydrate is not the first invention to blur the line between a natural process and a synthetic product, nor is it the first to engender confusion in the patent law. In the Nineteenth Century, the conflation of the natural acoustical principles of telephony with the invention of telephone equipment gave rise to massive litigation. *See Telephone Cases*, 126

U.S. 1, 8 S.Ct. 778, 31 L.Ed. 863 (1888). In disentangling this complex patent litigation, the Supreme Court noted that:

> In one of the cases on appeal . . . the court says: "There can be no patent for a mere principle. The discoverer of a natural force or a scientific fact cannot have a patent for that." But it proceeds to make this exception nugatory by confounding the natural process (or scientific fact) with the invented process for working the apparatus; sustaining the patent for the last upon a construction which blindly sweeps in the first.

Id. at 270-71, 8 S.Ct. 778. The '723 patent similarly confounds the scientific fact of paroxetine conversion with the invented product of paroxetine hemihydrate—and SKB similarly asks us to "sustain[ ] the patent for the last upon a construction which blindly sweeps in the first." *Id.* We should not only decline to do so, as the majority has and as the district court did in the alternative, but we should be clear about both the character and the implications of the underlying request.

Paroxetine hemihydrate is presumably a synthetic compound, created by humans in a laboratory, never before existing in nature, that is nevertheless capable of "reproducing" itself through a natural process. *SK II*, 247 F.Supp. 2d at 1022-23. This crystalline compound raises a question similar to one that might arise when considering the invention of a fertile plant or a genetically engineered organism, capable of reproduction, released into the wild. Consider, for example, what might happen if the wind blew fertile, genetically modified blue corn protected by a patent, from the field of a single farmer into neighboring cornfields. The harvest from those fields would soon contain at least some patented blue corn mixed in with the traditional public domain yellow corn—thereby infringing the patent. The wind would continue to blow, and the patented crops would spread throughout the continent, thereby turning most (if not all) North American

corn farmers into unintentional, yet inevitable, infringers.[7] The implication—that the patent owner would be entitled to collect royalties from every farmer whose cornfields contained even a few patented blue stalks—cannot possibly be correct. The underlying question that engaged the district court, and that led it to develop numerous alternative holdings, is *why* this implication is incorrect.

At oral argument, when faced with this hypothetical, SKB expressed its belief that such a blue-corn patent would be "very strong." Such a belief is misplaced. The implicit concept of "inevitable infringement" stems from the inevitable failure of the patent to provide public notice—which, in turn, stems from the inherently unpatentable nature of the claimed subject matter.

This section 101 problem therefore brings us full circle, back to the impossibility of public notice. Under normal circumstances, inventors other than the patentee will understand how to avoid infringing a patent by avoiding the claimed product. Because products, such as our hypothetical blue corn or SKB's paroxetine hemihydrate, that can be "made" through a natural process of spontaneous conversion imply inevitable infringement, no combination of claim language and written description could possibly teach even one skilled in the art how to avoid infringement. It is unsurprising that a requirement considered so trivial for most patentable products that we are content to let it remain implicit, namely a lesson in infringement avoidance, is effectively impossible for subject matter unpatentable under section 101. In short, patent claims drawn broadly enough to encompass products that spread, appear, and "reproduce" through natural processes

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[7] Although intent is not a factor in determining infringement, public notice is required as a predicate to the validity of a patent. *Jurgens v. CBK, Ltd.*, 80 F.3d 1566, 1570 n. 2 (Fed.Cir.1996). The hypothetical causes unavoidable infringement even in situations where the public would, in good faith, want to avoid infringing.

cover subject matter unpatentable under section 101—and are therefore invalid.

The majority asserts that a patentability analysis under section 101 does not consider whether a claimed product includes within its coverage naturally occurring compositions. The majority's view is not, and has never been, the law. Patentability "requires an examination of the contested claims to see if the claimed subject matter as a whole" comes within the subject matter described in section 101. *See AT&T Corp. v. Excel Communications, Inc.*, 172 F.3d 1352, 1357 (Fed.Cir.1999); *accord In re Alappat*, 33 F.3d 1526, 1557 (Fed.Cir.1994) (en banc). As this court has stated, "[t]he substantive issue at hand, whether the [patent] is invalid for failure to claim statutory subject matter under § 101, is a matter of both claim construction and statutory construction." *State Street Bank & Trust Co. v. Signature Fin. Group, Inc.*, 149 F.3d 1368, 1370 (Fed.Cir.1998). Both *AT & T* and *State Street* considered the scope of patent claims to determine their validity under section 101. The analysis provided by this concurrence is fully consistent with that approach.

Both *Animal Legal Defense Fund*, which the majority relies upon, and *Chakrabarty*, which *Animal Legal Defense Fund* relies upon, considered the patentability of "non-naturally occurring" organisms. *Animal Legal Def. Fund*, 932 F.2d at 927. The PTO rule at issue in *Animal Legal Defense Fund* announced that "nonnaturally occurring non-human multicellular living organisms" were patentable within section 101. *Id.* at 928. The same rule specifically announced that it "did not affect the principle that products found in nature will not be considered" patentable. *Id.* When the court, as the majority quotes, asserted that "[e]ither the subject matter falls within section 101 or it does not," it adverted to that underlying taxonomy. Whether subject matter is patentable under section 101 cannot be decided without classifying it as "nonnaturally occurring" or "found in nature."

Because the claimed PHC hemihydrate falls into both categories, it is not patentable under section 101. Merely limiting the claim to "synthetic PHC hemihydrate" would have solved the problem. But SmithKline Beecham did not.

VI.

Technological advances have forced this court, our predecessor court, and the Supreme Court to consider the line between the natural and the non-natural—including such inventions as non-naturally occurring plants and bacteria—several times over the past few decades. *See, e.g., In re Bergy*, 596 F.2d 952 (CCPA 1979), *rev'd sub nom Diamond v. Chakrabarty*, 447 U.S. 303, 100 S.Ct. 2204, 65 L.Ed.2d 144 (1980); *Pioneer Hi-Bred Int'l, Inc. v. J.E.M. Agric. Supply, Inc.*, 200 F.3d 1374 (Fed.Cir.2000), *aff'd* 534 U.S. 124, 122 S.Ct. 593, 151 L.Ed.2d 508 (2001). Paroxetine hemihydrate now appears to be the first patent litigated that forces the courts to consider the patentability of products and/or processes launched in a laboratory and released into nature.

Despite the complexity of the issue, the analysis is straightforward. An invention synthesized for the first time in a laboratory is eligible for patent protection under section 101. Processes for producing this synthetic product in the laboratory and/or for using this synthetic product may also be eligible for patent protection under section 101. However, a natural reproduction process, whether sexual, asexual, part of a chain reaction, or a process of decay, is ineligible for patent protection under section 101. *Chakrabarty*, 447 U.S. at 309, 100 S.Ct. 2204; *Funk Bros.*, 333 U.S. at 130, 68 S.Ct. 440. An item reproduced by such a natural process, whether an inorganic structure or a life form, must ipso facto be ineligible for patent protection under section 101.

The Supreme Court has cited with approval the Congressional Record surrounding the adoption of the Plant Patent Act of 1930:

> [A] plant discovery resulting from cultivation is unique, isolated, and is not repeated by nature, *nor can it be reproduced by nature unaided by man* . . . . " S.Rep. No. 315, supra, at 6; H.R.Rep. No. 1129, supra, at 7. Congress thus recognized that the relevant distinction was not between living and inanimate things, but between products of nature, whether living or not, and human-made inventions.

Chakrabarty, 447 U.S. 303, 100 S.Ct. 2204, 65 L.Ed.2d 144 (emphasis added). In its recent ruling confirming that hybrid plants are patentable subject matter under section 101, the Supreme Court noted that "[h]ybrid plants . . . generally do not reproduce true-to-type, i.e., seeds produced by a hybrid plant do not reliably yield plants with the same hybrid characteristics. Thus, a farmer who wishes to continue growing hybrid plants generally needs to buy more hybrid seed." *J.E.M.*, 534 U.S. at 128, 122 S.Ct. 593.

The principle unifying these statements about patentability made in 1930, 1980, and 2001, is that products capable of being "reproduced by nature unaided by man," *Chakrabarty*, 447 U.S. 303, 100 S.Ct. 2204, 65 L.Ed.2d 144, are not patentable subject matter under section 101. Though the parties have not briefed this question directly, they and the district court have provided more than sufficient facts to obtain a dispositive and incontrovertible legal determination that Claim 1 of the '723 patent is invalid under section 101.

The '723 patent, correctly construed, claims every single crystal of paroxetine hemihydrate, including those crystals arising through natural conversion. The district court properly admitted SKB's proffered expert testimony about the scientific mechanism underlying natural conversion, *SK II*,

247 F.Supp.2d at 1019-20, under *Daubert v. Merrell Dow Pharmaceuticals*, 509 U.S. 579, 113 S.Ct. 2786, 125 L.Ed.2d 469 (1993), and *General Electric v. Joiner*, 522 U.S. 136, 118 S.Ct. 512, 139 L.Ed.2d 508 (1997), weighed it in conjunction with contradictory testimony proffered by Apotex's experts, *SK II*, 247 F.Supp.2d at 1022, and concluded that at least some of Apotex's anhydrate would convert itself to hemihydrate. *SK II*, 247 F.Supp.2d at 1022- 23.

These findings lead to an inescapable conclusion—a conclusion that the majority attempts to dismiss as a question of "scope," rather than of patentability. Had SKB claimed "*synthetic* or *non-naturally occurring* crystalline paroxetine hydrochloride hemihydrate," the claim would have covered only patentable subject matter, and Apotex would be entitled to a judgment of noninfringement. Had SKB explicitly claimed the crystals converted in Apotex's facilities, as either "the *natural process* of converting paroxetine anhydrate to paroxetine hemihydrate" or "crystalline paroxetine hydrochloride hemihydrate *arising through natural conversion*," unpatentability under section 101 would be manifest; though the claimed matter would be a useful composition, it would be one that occurred in nature. *See Chakrabarty*, 447 U.S. at 309, 100 S.Ct. 2204; *Funk Bros.*, 333 U.S. at 130, 68 S.Ct. 440. By claiming simply "crystalline paroxetine hydrochloride hemihydrate" with no reference to how it was produced, SKB effectively claimed "crystalline paroxetine hydrochloride hemihydrate *whether non-naturally occurring or arising through natural conversion*." Claim 1, as issued, therefore combines patentable and unpatentable subject matter, and is invalid under section 101. The "confusion" to which the majority alludes should never arise because we cannot reach Section 102 unless the claimed matter can overcome the hurdle of section 101.

Inventors wishing to claim products that can either be synthesized in laboratories or generated by natural processes

may protect themselves by incorporating negative limitation terms like "non-natural" or "non-human" into the claims that they submit for examination. *See Amgen Inc. v. Hoechst Marion Roussel*, 314 F.3d 1313, 1329 (Fed.Cir.2003); *Animal Legal Def. Fund*, 932 F.2d at 923; *In re Wakefield*, 422 F.2d at 904. SKB made no such distinction. SKB, despite an early recognition of seeding and conversion, *SK II*, 247 F.Supp.2d at 1022, claimed all paroxetine hemihydrate crystals, including both those "born" of natural conversion without human intervention and those "made" in a laboratory through explicit human effort. SKB further demonstrated its claim to a possessory right in naturally occurring crystals by pursuing this litigation, and articulated this claim explicitly during oral argument.

The asserted breadth of Claim 1 makes sense only under the erroneous belief that patents may protect products spread and reproduced by natural processes, directly contradicting our well established understanding of the limits imposed by section 101. Given current scientific trends, such a belief could easily lead to misdirected research investments, to inappropriately issued patents, and to a widespread in terrorem effect crippling entire industries whose artisans learn that even their best efforts to respect patent rights may not save them from liability as inadvertent, inevitable infringers. As the district court recognized, the notice function of patents is meaningless in such an environment, *SK II*, 247 F.Supp.2d at 1028. The lack of suitable notice could easily chill innovation, inquiry, experimentation, and commercial development. The patent law does not sanction the concept of inevitable infringement.

Because SKB's assertion of the single crystal theory provides the correct construction of Claim 1, the '723 patent claims paroxetine hemihydrate crystals reproduced by nature unaided by man—unpatentable subject matter—and is therefore invalid under 35 U.S.C. § 101.

APPENDIX B

UNITED STATES COURT OF APPEALS
FEDERAL CIRCUIT

Nos. 03-2185, 03-1313

SMITHKLINE BEECHAM CORPORATION and
Beecham Group, P.L.C.,
Plaintiffs-Appellants,

v.

APOTEX CORP., Apotex, Inc., and Torpharm, Inc.,
Defendants-Cross Appellants.

April 8, 2005

Before MICHEL, *Chief Judge*, NEWMAN, MAYER, CLEVENGER, RADER, SCHALL, BRYSON, GAJARSA, LINN, DYK, and PROST, *Circuit Judges*.* NEWMAN, *Circuit Judge*, dissents in a separate order.

ON PETITION FOR REHEARING EN BANC.

ORDER

Petitions for rehearing *en banc* having been filed by both the Appellants-Cross-Appellees and Appellees-Cross-Appellants, responses thereto having been invited by the court and filed by both the Appellants-Cross-Appellees and Appellees-Cross-Appellants, and briefs of *amicus curiae* having been filed by Teva Pharmaceuticals USA, Inc. and Generic Pharmaceutical Association, the petitions for rehearing *en banc*, responses and briefs of *amicus curiae* having been referred to the circuit judges who are in regular active service, and a poll having been requested and taken,

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* LOURIE, *Circuit Judge*, did not participate in the vote.

IT IS ORDERED THAT:

(1) The petitions for rehearing *en banc* are granted for the limited purpose of vacating the panel's original opinion addressing the issue of experimental use. The panel's judgment and original opinion entered on April 23, 2004, as amended April 28, 2004, and reported at 365 F.3d 1306 (Fed.Cir.2004), is vacated.

(2) The case is remanded to the panel for further proceedings.

PAULINE NEWMAN, *Circuit Judge*, dissenting from the order declining rehearing *en banc*.

The court has granted the petitions for rehearing *en banc* for the limited purpose of remanding to the panel with regard to the issue of experimental use. I write to state my concern that the court has preserved the opinion's enlargement of the ground of invalidity called "inherent anticipation." The panel acknowledges that the hemihydrate had not been discovered until many years after the anhydrate product had been discovered and described in the '196 patent (United States Patent No. 4,007,196, filed July 23, 1975). The panel sustains the district court's findings that the hemihydrate was first discovered in March 1985 and may have existed in December 1984; how then can it have been "inherently disclose[d]," maj. op. at 18, in a patent application filed in 1975? Unlike any of the cases cited by the majority as ostensible precedent, there was no evidence whatsoever that the hemihydrate existed at the time the anhydrate patent application was filed, and no evidence that such existence would have been recognized by a person of skill in the field of the invention. These findings of chemical fact by this court are devoid of scientific support.

The district court's finding that it had not been established that the hemihydrate was produced in 1975 is in accord with the evidence, and surely has not been shown to be clearly

erroneous. There is no evidence to support the panel's current finding that the '196 patent "discloses in an enabling manner the production of the PHC hemihydrate." Maj op. at 20. The evidence before the district court did not show that disclosure and enablement, and did not show that the hemihydrate was produced in 1975, even inherently and undetected. The discovery of the hemihydrate a decade later, and the "seeding" of subsequent production in this crystal form, does not provide retrospective knowledge of this then-unknown compound. The not-unique situation that the air of the manufacturing plant is now seeded with the hemihydrate crystal form does not mean that this situation existed when the anhydrous product was discovered and the patent application thereon was filed.

Invalidity based on "anticipation," 35 U.S.C. § 102, requires that the identical invention was known or its existence would reasonably have been known to a person of ordinary skill in the field of the invention—not that it might have lain hidden in minuscule amount, undetected, unsuspected, and unknown. *See In re Oelrich,* 666 F.2d 578, 581, (CCPA 1981); *Hansgirg v. Kemmer,* 26 C.C.P.A. 937, 102 F.2d 212, 214 (CCPA 1939). The district court correctly found that there was not "clear and convincing evidence that the hemihydrate existed before the critical date of the '723 patent," maj. op. at 23, and on this finding the district court correctly ruled that there was not inherent anticipation. As summarized in *Continental Can Company USA v. Monsanto Company,* 948 F.2d 1264, 1269 (Fed.Cir.1991), "Inherency, however, may not be established by probabilities or possibilities. The mere fact that a certain thing may result from a given set of circumstances is not sufficient." The theory of inherent anticipation serves to accommodate "situations where the common knowledge of technologists is not recorded in the reference; that is, where technological facts are known to those in the field of the invention, albeit not known to judges." *Id.*

The panel now holds that a product that existed in trace amounts, although unknown and undetected and unisolated, is "inherently anticipated" and barred from the patent system after it is discovered. The patentability of antibiotics, hormones, antibodies, and myriad other previously unknown or unisolated products would be called into question by this new ruling, giving rise to uncertainty as to existing patents, as well as negation of searches for the beneficial components of existing materials. The breadth of the panel's theory of inherent anticipation contravenes long-established precedent. For example, in *Tilghman v. Proctor,* 102 U.S. (12 Otto) 707, 26 L.Ed. 279 (1880), the Supreme Court observed that it would be "absurd" to hold that a patent is anticipated because those skilled in the art later recognize that the discovery was "accidentally and unwittingly produced whilst the operators were in pursuit of other and different results, without exciting attention and without its even being known what was done or how it had been done." *See also Eibel Process Co. v. Minn. & Ont. Paper Co.,* 261 U.S. 45, 66, 43 S.Ct. 322, 67 L.Ed. 523 (1923) ("[A]ccidental results, not intended and not appreciated, do not constitute anticipation."). In *In re Seaborg,* 51 C.C.P.A. 1109, 328 F.2d 996 (CCPA 1964), our predecessor court rejected the "extrapolation" of the inherency theory to reach trace amounts of a nuclear isotope in a prior art process. *See id.* at 998-99 ("The record before us . . . is replete with showings that the claimed product, if it was produced in the Fermi process, was produced in such minuscule amounts and under such conditions that its presence was undetectable.").

Only after a compound is identified does it become subject to patenting; if its existence is not reasonably known to persons of skill in the field, its later discovery cannot be retrospectively "inherently anticipated."

APPENDIX C

UNITED STATES COURT OF APPEALS,
FEDERAL CIRCUIT

Nos. 03-1285, 03-1313.

SMITHKLINE BEECHAM CORPORATION and
Beecham Group, P.L.C.,
Plaintiffs-Appellants,

v.

APOTEX CORP., Apotex, INC., and Torpharm, Inc.,
Defendants-Cross Appellants.

April 23, 2004

Before RADER, BRYSON, and GAJARSA, *Circuit Judges.*

RADER, *Circuit Judge.*

Following a bench trial, the United States District Court for the Northern District of Illinois determined that the paroxetine hydrochloride anhydrate product produced by Apotex Corp., Apotex, Inc., and TorPharm, Inc. (collectively Apotex) will not infringe claim 1 of U.S. Patent No. 4,721,723 owned by SmithKline Beecham Corp. and Beecham Group, P.L.C. (collectively SmithKline). *SmithKline Beecham Corp. v. Apotex Corp.*, 247 F.Supp.2d 1011, 1052 (N.D.Ill.2003). Claim 1 of the '723 patent recites, in its entirety, "Crystalline paroxetine hydrochloride hemihydrate." Upon this court's revision of the trial court's erroneous claim construction, Apotex's product will infringe this claim. Nonetheless because the public use bar of 35 U.S.C. § 102(b) renders

claim 1 of the '723 patent invalid, this court affirms the district court's judgment in favor of Apotex.

I.

In the late 1970s, a British company called Ferrosan invented a new class of compounds, including a compound that became known as paroxetine. *See* U.S. Patent No. 4,007,196. The '196 patent claims paroxetine and its salts and discloses their antidepressant properties. Ferrosan eventually developed a process to produce the crystalline hydrochloride salt of paroxetine, or paroxetine hydrochloride (PHC). In 1980, Ferrosan licensed the '196 patent and its other PHC-related technology to SmithKline. SmithKline began manufacturing PHC in its Harlow plant in England.

In March 1985, a chemist in SmithKline's Worthing, England laboratory, Alan Curzons, created a new crystalline form of PHC while attempting to improve PHC production. Curzons' test results established that the new product was the hemihydrous form of PHC (PHC hemihydrate), while Ferrosan's original form was anhydrous PHC (PHC anhydrate). PHC anhydrate comprises crystals of PHC without bound water molecules. PHC hemihydrate comprises PHC crystals with one bound water molecule for every two PHC molecules. PHC hemihydrate proved more stable and thus more easily packaged and preserved.

Further review of the SmithKline samples showed that the Harlow plant had unwittingly made PHC hemihydrate as early as December 1984. In May 1985, SmithKline began double-blind clinical tests in the United States to determine the safety and efficacy of PHC hemihydrate capsules to treat depression symptoms. In these clinical tests, the doctors and patients were aware of the drug being tested, but were not aware which patients were taking a placebo and which were taking the actual drug.

SmithKline filed a patent application in the British Patent Office on October 25, 1985 relating to "crystalline paroxetine hydrochloride, its preparation and its uses as a therapeutic agent." The British application identified the invention as both the hemihydrate and the anhydrate form of PHC, as well as mixtures that contain a major portion of either form. One year later, on October 23, 1986, SmithKline filed a U.S. application claiming priority to the British application that issued as the '723 patent in 1988. The '723 patent does not claim PHC anhydrate and does not claim mixtures of the two PHC forms. The only claim at issue in this case is claim 1, which reads, "Crystalline paroxetine hydrochloride hemihydrate."

In 1993, after completing the necessary FDA approval process, SmithKline placed its antidepressant drug with PHC hemihydrate as the active ingredient on the market under the name Paxil®. In 1998, TorPharm, Inc., an Apotex affiliate and manufacturer of Apotex's generic antidepressant, filed an Abbreviated New Drug Application (ANDA) with the FDA, under 21 U.S.C. § 355(j), seeking approval to market its own PHC antidepressant drug. Apotex identified the active ingredient in its antidepressant as PHC anhydrate. Apotex's ANDA included a paragraph IV certification, *see* 21 U.S.C. § 355(j)(2)(A)(IV), that indicated Apotex intended to market the drug before the expiration of the '723 patent because its drug would not infringe that patent.

In 1998, SmithKline initiated this infringement action against Apotex under 35 U.S.C. § 271(e)(2) on the basis of Apotex's ANDA filing. SmithKline alleges that Apotex's proposed drug will infringe claim 1 of the '723 patent. SmithKline does not allege that claim 1 of the '723 patent covers PHC anhydrate. After all, PHC anhydrate—the Ferrosan discovery—is prior art for the '723 patent. SmithKline asserts that Apotex will infringe by manufacturing PHC anhydrate tablets that necessarily contain, by a conversion

process discussed below, at least trace amounts of PHC hemihydrate.

The parties filed various summary judgment motions, including cross motions for summary judgment that claim 1 of the '723 patent was invalid (or valid) under 35 U.S.C. § 102(b) for an impermissible public use. The § 102(b) motions acknowledged that the clinical trials occurred more than one year before SmithKline's filing date for the '723 patent, but disputed whether those tests qualified for the experimental use negation. The district court denied Apotex's motion and granted SmithKline's motion, holding that the '723 patent was not invalid for public use under § 102(b). The district court reasoned that the clinical trials qualified as experimental uses. *See SmithKline Beecham Corp. v. Apotex Corp.*, 286 F.Supp. 2d 925, 932-38 (N.D.Ill.2001).

The district court then held a bench trial to determine the proper interpretation of claim 1 and resolve the remaining infringement and validity issues. On the question of claim construction, the district court limited claim 1 to PHC hemihydrate in commercially significant amounts. *SmithKline Beecham Corp.*, 247 F.Supp.2d at 1030. The trial record contained uncontested testimony that a PHC anhydrate-hemihydrate mixture would need to possess a percentage of PHC hemihydrate in the "high double digits" if the hemihydrate component were to contribute any commercial value. *Id.* The district court grafted that commercial significance into the claim and held that Apotex's proposed PHC drug will not infringe claim 1 of the '723 patent. The district court found, as a factual matter, that Apotex's PHC anhydrate tablets will not contain detectable or commercially significant amounts of PHC anhydrate and rejected SmithKline's evidence to the contrary. *Id.* at 1031-39. The trial court also determined that claim 1 is not invalid.

SmithKline contested the district court's claim interpretation noting that claim 1 is clear on its face and encompasses

PHC hemihydrate in any amount, however small or insignificant. In rejecting that proposed claim interpretation, the district court also opined that SmithKline's proposed construction would render claim 1 indefinite. The district court reasoned that SmithKline's interpretation would place potential infringers in the untenable position of never knowing whether their product infringes because even a single undetectable crystal of PHC hemihydrate would infringe. *Id.* at 1029-30.

To show that manufacture of PHC anhydrate tablets necessarily creates PHC hemihydrate, SmithKline proffered expert testimony on the so-called "seeding" or "disappearing polymorph" theory. Under this theory, Ferrosan may have originally created a crystalline compound, namely PHC anhydrate, in a relatively unstable form. As Ferrosan and its successors improved the manufacturing and testing procedures for PHC, the compound "morphed" into a more pure and stable form, namely the PHC hemihydrate discovered in SmithKline's facilities. Once this new form or polymorph exists, SmithKline's experts explained, the general environment becomes "seeded" with crystals of the new polymorph. In this seeded environment, the old polymorph converts to the new polymorph upon its inevitable contact with seeds of the new polymorph. In other words, the creation of a pure version of the old polymorph becomes extremely difficult, if not impossible; the old polymorph has effectively disappeared and been replaced by the new.

SmithKline's experts applied the disappearing polymorph theory to show that Apotex's PHC anhydrate tablets inevitably convert to hemihydrate when combined with moisture, pressure, and practically ubiquitous PHC hemihydrate seeds. The district court found that SmithKline's evidence on seeding and the disappearing polymorph theory supported the inference that Apotex's PHC anhydrate tablets will contain at least trace, or undetectable, amounts of PHC hemihydrate.

Id. at 1042-43. Thus, under SmithKline's claim construction, the district court held that Apotex's PHC anhydrate drug would infringe claim 1 of the '723 patent. *Id.*

Alternatively, if claim 1 was construed to cover any amount of PHC hemihydrate and was, therefore, infringed, the district court purported to create a new equitable defense to infringement in favor of Apotex. *Id.* at 1043-45. Under this new defense, SmithKline was responsible for producing the hemihydrate, which, by virtue of SmithKline's disappearing polymorph theory, seeded the environment. Consequently, SmithKline caused the alleged infringement. The district court reasoned that Apotex should enjoy the right to practice the prior art by manufacturing PHC anhydrate. Accordingly, under its alternative equitable defense, the district court absolved Apotex of liability for the consequences of SmithKline's own conduct that rendered the practice of the prior art impossible without infringing the '723 patent. The district court also held that its inherent equitable powers and the equitable nature of injunctions in general placed the injunction mandated by 35 U.S.C. § 271(e)(4)(A) within the discretion of the district court. *Id.* at 1045-52.

SmithKline also sought to assert a claim of induced infringement against Apotex on the theory that anhydrate tablets convert to PHC hemihydrate in the stomach of a patient due to the increased humidity and pressure. The district court excluded SmithKline's evidence on this issue, finding that SmithKline would likely not meet its burden of showing "gastrointestinal infringement." *Id.* at 1014-15. Finally, the district court considered other alternative claim constructions, which would allow claim 1 to cover PHC hemihydrate in amounts detectable either by methods available at the time the '723 patent was filed or by any means that later became available. *Id.* at 1052. The record shows that SmithKline presented the results of tests on various samples of Apotex tablets. These tests showed PHC hemihydrate in the Apotex

product. The district court rejected this evidence as unreliable, mainly because SmithKline's counsel excluded select tablets from the testing without reasonable explanation. *Id.* at 1032-42. The trial court found these excluded tablets to represent best the product Apotex would manufacture upon ANDA approval. *Id.* Accordingly, the district court held that SmithKline did not prove that Apotex's tablets will contain any detectable amount of PHC hemihydrate.

SmithKline presents five arguments on appeal. First, the district court erred in limiting claim 1 to commercially significant amounts of PHC hemihydrate. Second, contrary to the trial court's ruling, a claim construction that covers PHC hemihydrate in any amount does not render claim 1 indefinite. Third, the district court erred in creating an equitable defense to infringement based on SmithKline's contribution to causing the infringement. Fourth, the district court erred in holding that the injunctive relief required under 35 U.S.C. § 271(e)(4) is within the district court's discretion. Fifth, the district court abused its discretion in excluding SmithKline's evidence of induced infringement.

In its cross-appeal, Apotex argues that the district court erred in granting summary judgment that SmithKline's clinical tests qualified as an experimental use. In particular, Apotex asserts that claim 1 of the '723 patent is invalid for public use under 35 U.S.C. § 102(b) as a matter of law. This court has jurisdiction over these appeals under 28 U.S.C. § 1295(a)(1).

II.

Standards of Review

This court reviews summary judgments without deference. *See Beech Aircraft Corp. v. EDO Corp.*, 990 F.2d 1237, 1245 (Fed.Cir.1993). Of course, a denial of summary judgment, by itself, is not a final judgment amenable to appeal like a grant of summary judgment. However, when both parties move for

summary judgment, each motion "must be independently assessed on its own merit." *California v. United States*, 271 F.3d 1377, 1380 (Fed.Cir.2001). In such circumstances, this court determines whether summary judgment is appropriate under the standard rules of Fed.R.Civ.P. 56.

In this case, both parties sought summary judgment; the district court granted one and denied the other. Thus, the record may show that the parties have conceded, and the district court has found, that no material factual issues remain in dispute. *See Beech Aircraft*, 990 F.2d at 1245. If this court determines that no material facts remain in dispute, it may proceed to determine entitlement to judgment under the law. *See Eli Lilly & Co. v. Barr Labs., Inc.*, 251 F.3d 955, 962 (Fed.Cir.2001) ("[R]eversal is required if the district court 'engaged in a faulty legal analysis in applying the law to the facts and a correct application of the law to those facts might bring a different result.'") (quoting *Litton Indus. Prods., Inc. v. Solid State Sys. Corp.*, 755 F.2d 158, 164 (Fed.Cir.1985)); *see also Anderson v. Liberty Lobby Inc.*, 477 U.S. 242, 248, 106 S.Ct. 2505, 91 L.Ed.2d 202 (1986).

This court reviews a district court's judgment, following a bench trial, for errors of law or clearly erroneous findings of fact. *See Allen Eng'g Corp. v. Bartell Indus., Inc.*, 299 F.3d 1336, 1343-44 (Fed.Cir.2002). Patent infringement proceeds under a two-step analysis. First, the court interprets the claims to determine their proper scope and meaning. *See Cybor Corp. v. FAS Techs., Inc.*, 138 F.3d 1448, 1454 (Fed.Cir. 1998) (en banc). Next, the court measures the accused product or process against the standard of the properly interpreted claims. *Id.*

This court reviews claim construction without deference. *See Markman v. Westview Instruments, Inc.*, 52 F.3d 967, 979, (Fed.Cir.1995) (en banc), *aff'd*, 517 U.S. 370, 116 S.Ct. 1384, 134 L.Ed.2d 577 (1996). This court reviews the second step, measurement of the accused product or process against

the claim, as a question of fact. *See Allen Eng'g*, 299 F.3d at 1343-44; *Gen. Mills, Inc. v. Hunt-Wesson, Inc.*, 103 F.3d 978, 981 (Fed.Cir.1997). The review of indefiniteness under 35 U.S.C. § 112, paragraph 2, proceeds as a question of law without deference. *See Solomon v. Kimberly-Clark Corp.*, 216 F.3d 1372, 1377 (Fed.Cir.2000); *Personalized Media Communications, LLC v. Int'l Trade Comm'n*, 161 F.3d 696, 702 (Fed.Cir.1998).

Factual Findings

As an initial matter, this court holds that the record supports the district court's factual findings. In particular, the district court did not clearly err in concluding that Apotex's PHC anhydrate product will include trace amounts of PHC hemihydrate based on the record evidence of seeding and disappearing polymorphs. *See SmithKline Beecham Corp.*, 247 F.Supp.2d at 1019-23.

The district court also did not clearly err in finding that Apotex's anhydrate product will not contain detectable quantities of PHC hemihydrate because SmithKline selectively tested the Apotex samples without explaining its reasons for excluding some Apotex products from the examination. Specifically, the district court's discretionary exclusion of SmithKline's unreliable evidence on this issue does not render the subsequent factual finding clearly erroneous. Accordingly, this court decides the legal issues in this appeal against the factual background as determined by the district court.

Claim Construction & Indefiniteness

Claim interpretation requires the court to ascertain the meaning of the claim to one of ordinary skill in the art at the time of invention. *ResQNet.com, Inc. v. Lansa, Inc.*, 346 F.3d 1374, 1378 (Fed.Cir.2003); *Phillips Petroleum Co. v. Huntsman Polymers Corp.*, 157 F.3d 866, 871 (Fed.Cir.1998). This task requires the court to place the claim language in its proper technological and temporal context. The best tools for

this enterprise are the various forms of intrinsic evidence and, when appropriate, extrinsic evidence. *See Vitronics, Corp. v. Conceptronic, Inc.*, 90 F.3d 1576, 1582 (Fed.Cir.1996). The intrinsic evidence, "i.e., the patent itself, including the claims, the specification and, if in evidence, the prosecution history . . . is the most significant source of the legally operative meaning of disputed claim language." *Id.*

Of course, at all times, the language of the claims governs their scope and meaning. *See Dow Chem. Co. v. Sumitomo Chem. Co.*, 257 F.3d 1364, 1372 (Fed.Cir.2001). Unless the intrinsic evidence compels a contrary conclusion, the claim language carries the meaning accorded those words in the usage of skilled artisans at the time of invention. *See id.; Vitronics*, 90 F.3d at 1582.

As stated earlier, claim 1 of the '723 patent reads, "Crystalline paroxetine hydrochloride hemihydrate." This language is not ambiguous, but rather describes a very specific compound. The record repeatedly shows that artisans in this area of technology at the time of invention would have understood that the claim embraces PHC hemihydrate without further limitation.

The inquiry proceeds to the remainder of the intrinsic record to determine if the patent applicant gave these unambiguous words some unexpected definition. The district court limited claim 1 to commercially significant amounts of PHC hemihydrate. The trial court found support for this limitation in portions of the '723 patent that discuss the pharmaceutical and commercial properties of PHC hemihydrate. For example, the specification discusses the superior handling properties of the hemihydrate form that improve the manufacture of PHC. Those references, however, do not redefine the compound in terms of its commercial properties, but emphasize that the new compound exhibits favorable characteristics. A description of characteristics does not redefine a compound with an established and unambiguous structural definition.

Moreover, nothing in the '723 patent limits that structural compound to its commercial embodiments. Rather, the '723 specification discloses PHC hemihydrate as a compound without reference to its commercial applications. For example, the specification states that the "present invention provides crystalline paroxetine hydrochloride hemihydrate as a novel compound." '723 patent, col. 1, ll. 57-58. Furthermore, nothing in the prosecution history of the '723 patent defines the invention in terms of commercially significant quantities. Thus, reading claim 1 in the context of the intrinsic evidence, the conclusion is inescapable that the claim encompasses, without limitation, PHC hemihydrate—a crystal form of paroxetine hydrochloride that contains one molecule of bound water for every two molecules of paroxetine hydrochloride in the crystal structure.

The district court openly discussed the policies that led to its insertion of commercially significant quantities as a limitation on the meaning of the claimed compound. The district court observed that a claim construction that covers trace amounts of PHC hemihydrate would likely preclude attempts to make the prior art PHC anhydrate compound. After explaining the "*in terrorem* effect" of such a "broad" claim construction, the district court rejected the literal scope of claim 1 because it would produce "absurd results" and would "not serve any policy of patent law." Claim construction, however, is not a policy-driven inquiry. As stated earlier, it is a contextual interpretation of language. The scope of patent claims can neither be broadened nor narrowed based on abstract policy considerations regarding the effect of a particular claim meaning. *See Quantum Corp. v. Rodime, PLC*, 65 F.3d 1577, 1584 (Fed.Cir.1995) ("[I]t is well settled that no matter how great the temptations of fairness or policy making, courts do not redraft claims"). For this precise reason, this court has repeatedly stated that a court must construe claims without considering the implications of covering a particular product or process. *See NeoMagic Corp. v.*

Trident Microsys. Inc., 287 F.3d 1062, 1074 (Fed.Cir.2002); *SRI Int'l. v. Matsushita Elec. Corp.*, 775 F.2d 1107, 1118 (Fed.Cir.1985).

The district court also justified its commercial-significance limitation to preserve the claim's validity in the face of a challenge to its definiteness under § 112, second paragraph. In essence, the district court considered the claim indefinite if construed to cover undetectable trace amounts of the PHC compound. In other words, the trial court feared that potential infringers would not be able to determine (and avoid) infringement if they cannot detect the claimed compound. *See Morton Int'l, Inc. v. Cardinal Chem. Co.*, 5 F.3d 1464, 1469-70 (Fed.Cir.1993). This reasoning misses the proper purpose of the definiteness requirement.

The second paragraph of § 112 requires the specification of a patent to "conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention." 35 U.S.C. § 112, ¶ 2 (2000). To satisfy this requirement, the claim, read in light of the specification, must apprise those skilled in the art of the scope of the claim. *See Miles Labs., Inc. v. Shandon, Inc.*, 997 F.2d 870, 875 (Fed.Cir.1993). Moreover, claims need not "be plain on their face in order to avoid condemnation for indefiniteness; rather, what [this court has] asked is that the claims be amenable to construction, however difficult that task may be." *Exxon Research & Eng'g Co. v. United States*, 265 F.3d 1371, 1375 (Fed.Cir.2001). In this case, the claim covers a definite chemical structure. To a chemist in this field, this claim is plain on its face. Thus, claim 1 of the '723 patent cannot be invalid for indefiniteness under § 112.

In *Morton*, this court affirmed a district court's judgment of indefiniteness because "one skilled in the art could not determine whether a given compound was within the scope of the claims." *Morton*, 5 F.3d at 1470. Thus, the claims at issue were "not sufficiently precise to permit a potential competitor

to determine whether or not he is infringing." *Id.* The *Morton* case, therefore, does not hold that the inability to detect the claimed compound in the infringing device renders a compound claim indefinite. Rather, *Morton* stands for the unremarkable proposition that a compound claim, to be definite, must apprise a skilled artisan of the bounds of the claim. The record in *Morton* contained "considerable evidence showing that those skilled in the art could not make the claimed compounds using the procedures of the specification, and no evidence that such compounds even exist." *Id.* at 1469-70.

This case bears little similarity to *Morton*. In this case, claim 1 unambiguously identifies the bounds of the claim. It states "Crystalline paroxetine hydrochloride hemihydrate." Thus, this claim recites in clear terms a discernible chemical structure. It would be difficult to imagine a more clear and definite claim.

The test for indefiniteness does not depend on a potential infringer's ability to ascertain the nature of its own accused product to determine infringement, but instead on whether the claim delineates to a skilled artisan the bounds of the invention. In this case, the problem for Apotex is that it cannot accurately ascertain the nature of its own product. The scope of this claim is clear; the infringement of the Apotex product is not. Even if a claim is broad enough to embrace undetectable trace amounts of the claimed invention, "[b]readth is not indefiniteness." *In re Gardner*, 57 C.C.P.A. 1207, 427 F.2d 786, 788 (CCPA 1970). Stated more precisely, this claim is neither broad nor narrow, but definitive of this particular chemical structure. For inventing and disclosing this structure, the inventor enjoys the exclusive right to practice that invention for the patent's limited term. Accordingly, claim 1, as construed above, is not indefinite under 35 U.S.C. § 112, second paragraph.

Infringement and Equity

Having interpreted claim 1 to cover PHC hemihydrate without further limitation, this court turns to infringement. In anticipation of this very scenario, the district court performed a factual infringement analysis based on this correct claim construction. The district court held that the evidence showed that Apotex's PHC anhydrate tablets would contain trace amounts of PHC hemihydrate. As indicated above, the record supports this factual finding. This court, therefore, affirms the district court's finding that Apotex's product will infringe under this court's claim construction.

Because Apotex seeks to practice the prior art, and because that practice infringes, the next logical inquiry involves anticipation. That is, if the prior art infringes now, logically the prior art should have anticipated the claim before the filing of the '723 patent. *See Bristol-Myers Squibb Co. v. Ben Venue Labs., Inc.*, 246 F.3d 1368, 1378 (Fed.Cir.2001) (re-stating the axiom that "that which would literally infringe if later in time anticipates if earlier"). At trial, Apotex asserted that Ferrosan's process of making PHC anhydrate inherently resulted in trace amounts of the hemihydrate prior to the '723 patent and thus anticipated that patent. The district court, however, determined that Apotex did not present clear and convincing evidence of inherent anticipation. According to the district court's findings, "no one knows when the hemi-hydrate form of paroxetine came into existence, although it is a reasonable inference that it did not exist in a detectable amount until" SmithKline's "serendipitous" discovery. *Smith-Kline Beecham Corp.*, 247 F.Supp.2d at 1022, 1025. Apotex does not appeal that ruling.

SmithKline's disappearing polymorph theory makes its apparently inconsistent positions possible. On the one hand, SmithKline asserts that the creation of a prior art compound will result in a product containing at least trace amounts of their patented compound. On the other hand, SmithKline

contends that the creation of the prior art compound before SmithKline's discovery of its compound did not have the same result. For this reason, the district court was understandably uncomfortable about allowing claim 1 to embrace its literal scope. The district court feared such a construction would result in "a considerable extension in the effective patent term of paroxetine because it might become difficult or even impossible to manufacture the pure anhydrous form after the Ferrosan patent expired." *Id.* at 1019. While these concerns are certainly legitimate, claim construction, as noted before, proceeds independent of its policy implications. Fortunately, the district court had the foresight to consider alternative analyses in this unique situation.

The district court, in its alternative infringement analysis, properly found infringement, but cabined the infringement with a new equitable defense. In short, the defense would apply where the patentee significantly contributed to causing the infringement. After all, SmithKline's creation of the hemihydrate form of PHC also created a seeded environment that, under the facts found by this district court, makes the practice of the prior art an infringement, while precluding operation of anticipation by inherency. In this unique and unprecedented circumstance, the trial court understandably reached out to find an equitable remedy to protect Apotex. In any event, notwithstanding the potential merit of a new equitable doctrine in this unprecedented instance, this court can resolve this case without its application because claim 1 is invalid for public use under 35 U.S.C. § 102(b). Accordingly, this court declines to address the trial court's proposed equitable defense.

The concurring opinion seeks to remedy the perceived inequity in this case by applying 35 U.S.C. § 101, arguing the subject matter of claim 1 does not cover patentable subject matter. Unfortunately, the concurrence confuses patent eligibility under § 101 with patentability under other provisions in

the Patent Act, such as 35 U.S.C. § 102. The concurrence admits that PHC hemihydrate is a synthetic, man-made compound eligible for patent protection. In fact, the claimed invention is without question a "composition of matter" or an article of "manufacture" within the terms of § 101. Accordingly, the claimed invention represents subject matter eligible for patent protection under § 101. With that conclusion, the inquiry under § 101 ends.

The concurring opinion, however, would expand the subject matter eligibility analysis under § 101 to encompass some review of the scope of the claims. To the contrary, "[e]ither the subject matter falls within Section 101 or it does not." *Animal Legal Def. Fund v. Quigg*, 932 F.2d 920, 930 (Fed.Cir.1991). The scope of the claims is not relevant to subject matter eligibility. Subject matter does not take on a different eligibility status with adjustments in the scope of the proposed claim. Patent eligibility under § 101 is simply not an issue in this case.

Public use—§ 102(b)

A patent claim is not valid if "the invention was . . . in public use . . . in this country, more than one year prior to the date of the application for patent in the United States." 35 U.S.C. § 102(b) (2000). Whether a patent is invalid due to public use under § 102(b) is a question of law based on underlying questions of fact. *See 3M Co. v. Chemque, Inc.*, 303 F.3d 1294, 1301 (Fed.Cir.2002). Thus, without genuine factual disputes underlying the public use inquiry, the issue is ripe for judgment as a matter of law.

In *Pfaff v. Wells Electronics, Inc.*, 525 U.S. 55, 119 S.Ct. 304, 142 L.Ed.2d 261 (1998), the Supreme Court rejected the former "substantially complete under a totality of circumstances" test for the on sale bar under § 102(b) and adopted a two-prong test. That test bars a patent when the claimed invention, before the critical date, was the subject of a

commercial offer for sale and was ready for patenting. *Id.* at 67, 119 S.Ct. 304. A similar analysis applies to the public use bar under § 102(b). Although the commercial sale prong is inapplicable, "[p]ublic use under 35 U.S.C. § 102(b) includes any use of the *claimed invention* by a person other than the inventor who is under no limitation, restriction or obligation of secrecy to the inventor." *Netscape Communications Corp. v. Konrad*, 295 F.3d 1315, 1321 (Fed.Cir.2002) (emphasis added). Thus, § 102(b) erects a bar where, before the critical date, the invention was ready for patenting and was used by a person other than the inventor who is under no confidentiality obligation.

"Experimental use negates public use; when proved, it may show that particular acts, even if apparently public in a colloquial sense, do not constitute a public use within the meaning of section 102." *Baxter Int'l, Inc. v. Cobe Labs., Inc.*, 88 F.3d 1054, 1059 (Fed.Cir.1996) (citing *TP Labs., Inc. v. Prof'l Positioners, Inc.*, 724 F.2d 965, 971 (Fed.Cir.1984)); *see also City of Elizabeth v. Am. Nicholson Pavement Co.*, 97 U.S. 126, 134, 24 L.Ed. 1000 (1877). The experimental use doctrine is not an "exception" to the public use bar because it does not shift the burden of proof from the accused infringer to the patentee. Rather, it operates to negate application of the public use bar. *See EZ Dock, Inc. v. Schafer Sys., Inc.*, 276 F.3d 1347, 1351-52 (Fed.Cir.2002) ("This court has repeatedly stressed that evidence of experimental use does not give rise to a free-standing doctrinal exception to statutory bars, but instead operates to negate application of section 102(b)").

In other words, once the challenger of the patent has proven by clear and convincing evidence that the invention was in public use before the critical date, the burden of production shifts to the patentee to provide sufficient evidence to create a genuine issue of material fact that the use qualifies as experimental. The ultimate burden, however, remains on the

challenger to prove by clear and convincing evidence that the non-experimental use was public under § 102(b). *Id.*

With these burdens and legal standards in mind, this court agrees with the district court and the parties that no material facts relating to the public use bar are in dispute. The record shows that PHC hemihydrate was in public use before the critical date of the '723 patent. Specifically, SmithKline placed PHC hemihydrate in public clinical trials in the United States in May 1985. The critical date under § 102(b) for the '723 patent is October 23, 1985. Moreover, SmithKline administered PHC hemihydrate to patients without any apparent confidentiality restrictions on the patients or the administering physicians. SmithKline does not question the public disclosure of its clinical trials. Rather, SmithKline asserts that the clinical trials constitute an experimental use negating the apparent public use. In SmithKline's own words, the purpose of the clinical trials was "to establish that [PHC hemihydrate] actually worked (and was safe) as an antidepressant."

Taking the facts in the light most favorable to SmithKline, this court assumes that the clinical trials were subject to satisfactory controls and otherwise properly conducted to fulfill their intended purpose—namely, to establish the efficacy and safety of PHC hemihydrate as an antidepressant drug for humans. The determinative inquiry in this case is whether SmithKline tested the invention of the asserted claim. "[T]esting or experimentation performed with respect to non-claimed features of the device does not show that the *invention* was the subject of experimentation." *W. Marine Elecs., Inc. v. Furuno Elec. Co.*, 764 F.2d 840, 847 (Fed.Cir. 1985). In other words, an experimental use only negates a statutory bar when the inventor was testing claimed features of the invention. *In re Theis*, 610 F.2d 786, 793 (CCPA 1979) ("It is settled law that . . . [an] experimental sale . . . does not apply to experiments performed with respect to non-claimed

features of an invention."); *LaBounty Mfg. Inc. v. U.S. Int'l Trade Comm'n.*, 958 F.2d 1066, 1074 (Fed.Cir.1992); *In re Brigance*, 792 F.2d 1103, 1109 (Fed.Cir.1986).

Indeed the Supreme Court case that created the experimental use negation, *City of Elizabeth*, 97 U.S. at 126, acknowledged the purpose of this doctrine: "The use of an invention by the inventor himself, or of any other person under his direction, by way of experiment, and in order to bring the invention to perfection, has never been regarded as such a [public] use." In other words, the doctrine extends to experimentation on the claimed invention to bring it to perfection. The negation does not extend beyond the claimed invention or beyond the purpose of perfecting the invention. *See, e.g., In re Smith*, 714 F.2d 1127 (Fed.Cir.1983) ("[E]xperimental use . . . does not include market testing").

This court has already defined the invention of claim 1 as the PHC hemihydrate compound without further limitation regarding efficacy, commercial use, or pharmaceutical viability. SmithKline itself espouses that proper claim construction. With that definition of the invention in mind, however, clinical trials designed to establish the efficacy and safety of the compound as an antidepressant for FDA approval are not experimental uses of that claimed invention. In other words, the claim covers the compound regardless of its use as an antidepressant. The antidepressant properties of the compound are simply not claimed features. Consequently, the clinical tests, which measured the efficacy and safety of the compound as an antidepressant, did not involve the claimed features of the invention. The 1985 clinical tests, therefore, do not qualify as an experimental use to negate the statutory bar.

In making this ruling, this court is aware of cases that acknowledged an experimental use negation when the testing did not focus on an expressly claimed feature. *See EZ Dock*, 276 F.3d at 1353; *Seal-Flex, Inc. v. Athletic Track & Court*

Constr., 98 F.3d 1318, 1320, 1324 (Fed.Cir.1996) ; *Manville Sales Corp. v. Paramount Sys., Inc.*, 917 F.2d 544, 550-51 (Fed.Cir.1990). To some extent, this apparent confusion arises from a separate requirement of patent law to test an invention for utility, i.e., to show that it works for its intended purpose. *See Scott v. Finney*, 34 F.3d 1058, 1061 (Fed.Cir.1994). This court has noted the potential overlap of utility and experimental use testing. *EZ Dock*, 276 F.3d at 1352. As suggested by their different origins and purposes, however, utility testing (reduction to practice) and experimental use testing are not synonymous.

Testing to reduce an invention to practice shows completion of an invention and establishes its utility. *See, e.g., Holmwood v. Sugavanam*, 948 F.2d 1236 (Fed.Cir.1991). The focus is on whether the totality of the testing at the relevant time period was sufficient to prove an actual reduction to practice of the invention. *See Scott*, 34 F.3d at 1061-62. Experimental testing, on the other hand, negates evidence that an inventor has fatally postponed filing beyond a bar date. *See City of Elizabeth*, 97 U.S. at 126. Here, the focus is on whether the specific testing in question was necessary to reduce the claimed invention to practice. That is, after the invention is reduced to practice, further testing will not qualify as experimental use for purposes of negating a bar under § 102(b). *See Continental Plastic Containers v. Owens Brockway Plastic Prods.*, 141 F.3d 1073, 1079 (Fed. Cir. 1998) ("The policy behind experimental use negation is to give the inventor an opportunity to reduce the invention to practice. . . . Thus, experimental use can not occur after a reduction to practice") (citations omitted).

Due to these different origins and purposes, the narrower experimental use negation does not extend beyond perfecting claimed features. In any event, even the cases above that acknowledge experimentation on features beyond those expressly claimed remain faithful to these strict limits of the

experimental use negation. Each of those cases permitted testing to negate the bar when the experimentation improves or verifies a feature inherent in the express claims of the invention.

In *Manville*, for example, the claimed invention covered a light pole for highways that maintenance workers could lower for repairs. *See* 917 F.2d at 547-48. At the outset, this court decided *Manville* on the basis that the applicant retained the invention confidential and at no time placed it in the public domain. *Id.* The purported experimental use tested the illuminating device under severe weather conditions. Neither party asserted that this experimentation exceeded the literal scope of the claims, probably because the use occurred in a remote Wyoming rest area not yet open to the public at the top of a 150-foot pole. Indeed this court noted: "Manville did nothing to lead the public to believe that its iris arm invention was in 'the public domain.'" *Manville*, 917 F.2d at 549. In other words, the use was either not public or properly confidential. This court also noted: "Manville marked its design drawing with a confidentiality notice." *Id.* To the limited extent that this case also relied on the experimental use negation, this court explained: "[D]urability in an outdoor environment is inherent to the purpose of the invention." *Id.* at 551. Thus, the experimentation verified features inherent in the claimed invention.

In *Seal-Flex*, the claimed invention covered an all-weather activity mat (or track). *Seal-Flex*, 98 F.3d at 1320-21. The patentee alleged that the product it sold was not the completed invention because it was still being tested for its performance in harsh weather conditions. *Id.* At the outset, it is significant to note that this court decided *Seal-Flex* under standards for public use overruled by *Pfaff*. Therefore, this court weighed a "totality of circumstances" that no longer apply. *Id.* at 1322-23. Again, the parties did not raise the issue of limiting testing to claimed features. Like the *Man-*

ville case, however, the scope of the claimed invention in *Seal-Flex* carried the inherent implication of performance in severe weather conditions. It was an all-weather track. *Id.* at 1324. Thus, the experimentation again focused on features inherent to the claimed invention. Importantly, this court in *Seal-Flex* did not affirmatively find that there was no on-sale bar under § 102(b) or that the activities constituted an experimental use. Rather, this court vacated the district court's summary judgment and remanded the case. *Id.*

In *EZ Dock*, the claim covered a "floating dock." *EZ Dock*, 276 F.3d at 1348. The testing involved the dock's performance in rough, choppy water. *Id.* at 1353. Although the claim did not have an express "choppy water" limitation, the claim language "floating dock" carried the implication that the invention must perform in rough water. Thus, again, the experimentation verified or improved a feature inherent to the claimed invention. Again, the court vacated the summary judgment of invalidity and remanded for determination of the on-sale bar and experimental use issues. *Id.* at 1353-54. In sum, this court has remained faithful to the strict requirements of the experimental use negation by limiting it to testing to perfect claimed features, or, in a few instances, testing to perfect features inherent to the claimed invention.

In this case, SmithKline's experimentation does not fit within the rule limiting the negation to tests on claimed features. *See In re Theis*, 610 F.2d at 793. In connection with the claim interpretation issue, SmithKline strenuously argues that nothing in the claim language, the specification, or the prosecution history indicates that the scope of claim 1 implicates any intended commercial significance or medical purpose. In fact, the claim does not carry any implication of commercial significance or medical purpose. While SmithKline benefits from the breadth of the meaning of its claim, that claim does not require testing tailored to ascertain the safety and effectiveness of a particular use. Thus, testing the

medical efficacy and viability of PHC hemihydrate is not testing the claimed features of the structural invention in claim 1.

SmithKline's assertion that the clinical tests constituted an experimental use of the invention of claim 1 is inconsistent with its claim construction position. This court also notes that these same clinical trials may serve to negate a public use bar with regard to the inventions claimed in the more specific claims of the '723 patent. Only claim 1, however, is before the court in this appeal. Nothing in the language of claim 1 can reasonably be read to carry an implication that the claimed compound will be used as an anti-depressant, or even a pharmaceutical for that matter. Because claim 1 covers the compound without further limitation, the invention of claim 1 was reduced to practice when that compound was first manufactured. Its efficacy as an anti-depressant is irrelevant to that determination.

Accordingly, a patentee should understand that testing the properties, uses, and commercial significance of a compound claimed solely in structural terms may start the clock under § 102(b) for filing a claim that is not limited by any property, commercially significant amount, or other use of the compound. Because these clinical trials tested only the safety and efficacy of PHC hemihydrate as an antidepressant, those trials were not an experimental use of the invention in claim 1. Consequently, this court determines that claim 1 of the '723 patent is invalid for public use under § 102(b) as a matter of law. This court reverses the district court's grant of summary judgment of validity in favor of SmithKline and reverses the district court's denial of summary judgment of invalidity in favor of Apotex.

Miscellaneous Issues

SmithKline also appealed the district court's decision to prevent SmithKline from pursuing its contributory infringe-

ment claim. In essence, that claim asserted that the ingestion of Apotex's PHC anhydrate tablet by a patient would result in conversion to the hemihydrate. In the interim, this court decided *Schering Corp. v. Geneva Pharmaceuticals, Inc.*, 339 F.3d 1373 (Fed.Cir.2003). In that case, this court determined that a compound claim was anticipated due to evidence that a prior art substance metabolized into the claimed compound upon ingestion by a patient. Recognition of the conversion process at the time of the prior art was not necessary to prove inherent anticipation. *Id.* at 1379-81. Thus, if SmithKline proved contributory infringement by showing that PHC anhydrate metabolizes into PHC hemihydrate upon ingestion, SmithKline may also have proved that PHC hemihydrate was inherent in the prior art. Nevertheless, because claim 1 is invalid for public use under § 102(b), SmithKline's appeal concerning its contributory infringement claim is moot.

Similarly, SmithKline's appeal of the district court's ruling that injunctive relief under 35 U.S.C. § 271(e)(4) is within the district court's discretion is also moot. That ruling was not necessary for the district court's judgment below and is immaterial to the determination of this appeal. This court, therefore, does not address that issue in this opinion.

III.

In summary, this court reverses the claim construction of the district court and holds that claim 1 covers any amount of crystalline paroxetine hydrochloride hemihydrate without further limitation. Based on the factual findings of the district court, this court affirms the district court's finding that Apotex's PHC anhydrate product will infringe claim 1 under that broad construction. Notwithstanding that conclusion, this court holds, based on the undisputed facts, that SmithKline's clinical trials constituted a public use under § 102(b) rendering claim 1 invalid. Apotex is, therefore, not liable for infringing claim 1 of the '723 patent. This court affirms the district court's judgment.

COSTS

Each party shall bear its own costs.

AFFIRMED.

GAJARSA, *Circuit Judge*, concurring.

I concur in the court's judgment finding Claim 1 of the '723 patent invalid, however, I reach the judgment by a different statutory provision. I would find Claim 1 invalid because it encompasses subject matter that is unpatentable under 35 U.S.C. § 101.[1]

I.

A. *Authority*

The question of patentability under Section 101 does not arise often, and a court's decision to raise it sua sponte is even less common. The centrality of patentable subject matter to the entire scope of the patent law suggests that there are times when such inquiries are critical. The Supreme Court established long ago that "the question whether the invention, which is the subject-matter in controversy, is patentable or not is always open to the consideration of the court, whether the point is raised by the answer or not." *Slawson v. Grand St. R.R.*, 107 U.S. 649, 652, 2 S.Ct. 663, 27 L.Ed. 576 (1882). *See also Richards v. Chase Elevator Co.*, 158 U.S. 299, 301, 15 S.Ct. 831, 39 L.Ed. 991 (1895). These precedents remain good law, though the courts have relied upon them infrequently. The policy that drove them, however, remains vibrant. Less than a decade after *Slawson*, in the context of an interference, the Supreme Court stressed that though

> [t]he parties to the present suit appear to have been willing to ignore the question as to patentability in the present case, and to have litigated merely the question of priority of invention, on the assumption that the inven-

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[1] "Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title." 35 U.S.C. § 101.

> tion was patentable. But neither the Circuit Court nor this court can overlook the question of patentability.

Hill v. Wooster, 132 U.S. 693, 698, 10 S.Ct. 228, 33 L.Ed. 502 (1890). In contemporary patent law, 37 C.F.R. § 1.641 specifically allows an administrative patent judge to raise the issue of patentability sua sponte as to claims designated to correspond to a count of an interference.

Beyond administrative proceedings, courts have found the occasional need to raise Section 101 issues sua sponte—even subsequent to the 1952 revisions to the Patent Act. At least three of our sister circuits, whose rulings on patent law prior to 1982 do not bind this court but retain persuasive value, raised Section 101 issues that the parties had not addressed. The Ninth Circuit announced that "it is the duty of the court to dismiss a patent infringement suit whenever it affirmatively appears that the patent is invalid." *Barkeij v. Lockheed Aircraft Corp.*, 210 F.2d 1, 2 (9th Cir.1954). According to the Second Circuit, "[e]ven were section 101 not raised by appellees, it was not error for the district court to consider it since it had the power to do so. Section 101 deals with the subject matter of patents and, as such, it is always open to the consideration of the court . . ." *Howes v. Great Lakes Press Corp.*, 679 F.2d 1023, 1028 (2d. Cir.1982). And the Third Circuit explained that

> [i]t has been clear from an early date, that the court could dismiss a bill because the invention described in the patent was not patentable, even when no defense of invalidity was set up in the answer. . . . Accordingly, when a party brings suit on a patent alleging infringement, it is accountable for the validity of the patent. . . .

Borden Co. v. Clearfield Cheese Co., 369 F.2d 96, 99-100 (3d. Cir.1966).

The Federal Circuit has independently raised Section 101 concerns without prompting from the parties at least once

before. In *Titanium Metals Corp. v. Banner*, 778 F.2d 775 (Fed.Cir.1985), we considered a patent that the PTO had rejected as both anticipated under Section 102 and obvious under Section 103. *Id.* at 776. The district court reversed, and issued an order authorizing the Commissioner of Patents and Trademarks to issue the patent. *Titanium Metals Corp. v. Mossinghoff*, 603 F.Supp. 87, 91 (D.D.C.1984). The government appealed. The matter therefore reached this court on issues relevant to Sections 102 and 103, not to Section 101. We explained, however, that

> [t]he patent law imposes certain fundamental conditions for patentability, paramount among them being the condition that what is sought to be patented, as determined by the claims, be new. The basic provision of Title 35 applicable here is § 101 . . . The title of the application here involved is "Titanium Alloy," a composition of matter. Surprisingly, in all of the evidence, nobody discussed the key issue of whether the alloy was new, which is the essence of the anticipation issue. . . .

Titanium Metals, 778 F.2d at 781. We concluded that "the decision and order of the district court holding that claims 1, 2, and 3 are directed to patentable subject matter and authorizing the issuance of a patent thereon were clearly erroneous and are reversed." *Id.* at 783. In other words, we recognized that we could neither affirm nor reverse the district court's holdings under Sections 102 and 103 in a principled way without addressing the underlying erroneous assumption that the invention at issue met the requirements of Section 101. *See also Brassica Protection Prods. LLC v. Sunrise Farms (In re Cruciferous Sprout Litig.)*, 301 F.3d 1343, 1350 (Fed. Cir.2002) (characterizing as "common sense" *Titanium Metals*' rationale, including the injection of Section 101 into an anticipation analysis).

Both this court and the Supreme Court have recognized that there is a significant public policy interest in removing

invalid patents from the public arena. In *Cardinal Chemical Co. v. Morton International, Inc.*, 508 U.S. 83, 100, 113 S.Ct. 1967, 124 L.Ed.2d 1 (1993), the Supreme Court reversed our practice of vacating findings of invalidity where the court found non-infringement in light of the strong public interest in resolving questions of patent validity. In *Blonder-Tongue Labs., Inc. v. University of Illinois Foundation*, 402 U.S. 313, 91 S.Ct. 1434, 28 L.Ed.2d 788 (1971), the Supreme Court commented at length on the wasteful consequences of relitigating the validity of a patent after it has once been held invalid. In *United States v. Glaxo Group, Ltd.*, 410 U.S. 52, 57-58, 93 S.Ct. 861, 35 L.Ed.2d 104 (1973), the Supreme Court ruled that the government, like patent licensees, could always challenge the validity of a patent in the course of prosecuting an antitrust action "to vindicate the public interest in enjoining violations of the Sherman Act." The Court cited numerous cases[2] as "sufficient authority" to support this holding, *id.*, which it saw as furthering a longstanding policy orientation: "It is as important to the public that competition should not be repressed by worthless patents, as that the patentee of a really valuable invention should be protected in his monopoly. . . ." *Pope Mfg. Co. v. Gormully*, 144 U.S. 224, 234, 12 S.Ct. 632, 36 L.Ed. 414 (1892).

These decisions mirror our own recognition that "[p]ublic policy requires that only inventions which fully meet the statutory standards are entitled to patents." *Constant v. Advanced Micro-Devices, Inc.*, 848 F.2d 1560, 1564 (Fed.Cir.1988)

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[2] *Telephone Cases*, 167 U.S. 224, 17 S.Ct. 809, 42 L.Ed. 144 (1897); *United States v. U.S. Gypsum Co.*, 333 U.S. 364, 68 S.Ct. 525, 92 L.Ed. 746 (1948); *Sola Elec. Co. v. Jefferson Elec. Co.*, 317 U.S. 173, 63 S.Ct. 172, 87 L.Ed. 165 (1942); *Edward Katzinger Co. v. Chicago Metallic Mfg. Co.*, 329 U.S. 394, 67 S.Ct. 416, 91 L.Ed. 374 (1947); and *MacGregor v. Westinghouse Elec. & Mfg. Co.*, 329 U.S. 402, 67 S.Ct. 424, 91 L.Ed. 380 (1947); *Pope Mfg. Co. v. Gormully*, 144 U.S. 224, 234, 12 S.Ct. 632, 36 L.Ed. 414 (1892); *Lear, Inc. v. Adkins*, 395 U.S. 653, 670, 89 S.Ct. 1902, 23 L.Ed.2d 610 (1969).

(citations omitted), and that "[t]here is a stronger public interest in the elimination of invalid patents than in the affirmation of a patent as valid." *Nestier Corp. v. Menasha Corp.-Lewisystems Div.*, 739 F.2d 1576, 1581 (Fed.Cir.1984). The best way to ensure that patents issue only for inventions in full compliance with the statutory standards is to allow "the validity of a patent, which was originally obtained in ex parte proceedings in the PTO, [to] be challenged in court." *Constant*, 848 F.2d at 1564.

My belief that this case warrants a sua sponte Section 101 inquiry therefore falls well within a long if somewhat sparse tradition, driven in part by concerns of public policy but grounded entirely in legal authority. Where, as here, the facts are both unusual[3] and undisputed, where the legal implication of these facts is clear, and where a consideration of fundamental aspects of law and policy is necessary to maintain the integrity of the patent law, a sua sponte inquiry into the patentability of the claimed subject matter is appropriate.

B. *Claim Construction and Prior Use*

Before discussing my reasons for finding Claim 1 of the '723 Patent invalid for claiming unpatentable subject matter, however, I do need to address a few preliminary matters. I

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[3] The district court's maze of alternative claim constructions and theories finding Apotex not liable for infringement, plus the theory added by the majority, attest to the unique circumstances of this case. The district court's opinion, and in particular its attempt to introduce a novel equitable defense, *SmithKline Beecham Corp. v. Apotex Corp.*, 247 F.Supp.2d 1011, 1043-45 (N.D.Ill.2003) ("*SK II*"), strongly imply that something "feels wrong" about holding an infringer liable for inevitable, spontaneous infringement. We therefore face a choice. We can either address the issue head-on and explain why an attempt to patent unpatentable subject matter leads to so many apparent anomalies, or we can try to contort the aspects of patent law raised by the parties in order to avoid those anomalies. I believe that the law is best served by adopting the straightforward approach.

agree with the majority that the "single crystal" theory[4] provides the only construction that is entirely consistent with the Claim 1's language claiming "crystalline paroxetine hydrochloride hemihydrate" ("paroxetine hemihydrate"). I also agree with the majority that the paroxetine hemihydrate "made" in Apotex's seeded manufacturing facilities through the natural conversion of the off-patent paroxetine anhydrate and water vapor present a prima facie case of infringement.

I agree with the district court, however, that SKB is entitled to summary judgment that the '723 patent is not invalidated by prior public use, *SmithKline Beecham v. Apotex Corp.*, 286 F.Supp.2d 925, 938 (N.D.Ill.2001) ("SK I"), because "the control [SKB] actually exercised over the trials was sufficient to demonstrate that the trials were in the nature of experimentation rather than mere commercial use," *id.* at 934, and because SKB's experiments designed to assess the product's efficacy as an antidepressant, *id.* at 932, were relevant to the '723 patent in the same way that the experimental use doctrine preserved the validity of the patents in our previous cases. *See Manville Sales Corp. v. Paramount Sys. Inc.*, 917 F.2d 544, 550 (Fed.Cir.1990); *Seal-Flex, Inc. v. Athletic Track & Court Constr.*, 98 F.3d 1318

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[4] The district court defined the "single crystal" theory of Claim 1 as encompassing:

> *all* manifestations of the hemihydrate, no matter how or where produced, or in what quantity relative to the mixture of which it is a part; even if the production was inadvertent, unavoidable though undesired, and wholly without benefit to the producer or detriment to SmithKline in the sense of cutting into SmithKline's market; and even if the amount is so tiny as to be beyond the limits of detection of any instrument present or foreseeable and the product in which it unexpectedly pops up does not compete with anything made or sold by SmithKline.

SK II, 247 F.Supp.2d at 1026 (emphasis in original).

(Fed.Cir.1996); *EZ Dock, Inc. v. Schafer Sys. Inc.*, 276 F.3d 1347 (Fed.Cir.2002).

In *EZ Dock*, for example, the patent at issue claimed a polyethylene floating dock—like the claim at issue here, a product claim. *Id.* at 1348. The district court determined that the patentee had offered the claimed dock for sale in the United States. more than one year before filing the patent application. *Id.* at 1350. We noted that though the defendant had presented a prima facie case against EZ Dock, EZ Dock's evidence could convince a jury that the sales were experimental. *Id.* at 1352. We explained that though the "experiments" did not test features actually claimed in the patent, an experimental use defense was still available because "[the inventor] testified that he sold the dock . . . to determine whether it was capable of performing its intended purpose in its intended environment." *Id.* at 1353.

We noted that this application of the experimental use doctrine, like our earlier assessment of experimental use in *Manville*, 917 F.2d at 550, extended the notion of experimentation beyond features claimed explicitly in the patent to include the *intended purpose* of those features. *EZ Dock*, 276 F.3d at 1353. The majority notes this extension with approval, and attempts to distinguish the present matter from our precedent by focusing on reduction to practice. According to the majority, SKB's testing of paroxetine hemihydrate's performance as a human antidepressant was not necessary to reduce paroxetine hemihydrate to practice. The majority does not make clear, however, why testing a light pole's performance at illumination under severe weather conditions was necessary to reduce the light pole to practice, *Manville*, 917 F.2d at 547-48, why testing an all-weather activity mat's performance in harsh weather was necessary to reduce the mat to practice, *Seal-Flex*, 98 F.3d at 1320-21, or why testing a floating dock's performance in rough, choppy water was necessary to reduce the dock to practice, *EZ-Dock*,

276 F.3d at 1353-54. In all four cases, the claims at issue were product claims that did not claim the tested features explicitly. In all four cases, the patentees possessed the claimed product in substantial enough form to test their products' performance at their intended functions. The majority does not explain why only one of these four patentees had reduced its claimed invention to practice sufficiently to preclude the experimental use doctrine. I see no principled grounds on which to distinguish this case from our precedent. *See Manville*, 917 F.2d at 550; *Seal-Flex*, 98 F.3d at 1324; *EZ Dock*, 276 F.3d at 1353. The district court was correct in finding that, under our precedent, the prior-use bar did not invalidate the '723 Patent. *SK I*, 286 F.Supp.2d at 938. The majority seems to be trying to reach an ultimate conclusion of invalidity while avoiding the road less traveled.

Nevertheless, because the district court misconstrued the claim, I cannot share its conclusion that Claim 1 is "valid against the various attacks on it made by Apotex." *SmithKline Beecham Corp. v. Apotex Corp.*, 247 F.Supp.2d 1011, 1052 (N.D.Ill. 2003) ("*SK II*"). Claim 1 of the '723 patent is invalid because it is broad enough to claim subject matter that is unpatentable under Section 101. The troubling implications of this impermissible breadth explain the various anomalies that engaged the district court. Under normal circumstances, patented products do not simply "appear" in ways that convert noninfringing products into infringing products.

The district court found as a matter of fact that paroxetine hemihydrate is an exception to this general rule. *SK II*, 247 F.Supp.2d at 1022-23. I agree with the majority that the record supports the district court's factual findings, and that these findings provide the appropriate background for our legal conclusions—specifically including the district court's findings concerning seeding and conversion.

II.

A. *Theory of Infringement*

Because the proper construction of Claim 1 follows the "single crystal" theory, SKB must prove that Apotex's product does and will continue to contain at least some hemihydrate. Though SKB's legal burden is only to prove infringement by a preponderance of the evidence, *S. Bravo Systems, Inc. v. Containment Technologies. Corp.*, 96 F.3d 1372, 1376 (Fed.Cir.1996), SKB nevertheless faces a significant challenge. As the district court found, Apotex wants to manufacture pure anhydrate; any hemihydrate present in its product is an undesirable impurity. *See SK II*, 247 F.Supp.2d at 1015, 1025, 1045. Both SKB and the district court explicitly rejected the possibility that the anhydrous and hemihydrous forms of paroxetine came into existence simultaneously, and that every batch of paroxetine ever manufactured (or that ever will be manufactured) contains at least trace elements of hemihydrate—an argument that would not only prove SKB's point about Apotex's product, but would also invalidate the '723 Patent as inherent in the prior art. *Id.* at 1025.

SKB's basic theory of infringement, which the district court recognized as establishing a prima facie case of infringement when applied to the single crystal construction, *id.* at 1043, rests upon two scientific principles that remain matters of controversy within the scientific community, both as general phenomena and as applied to paroxetine: seeding and conversion. *See id.* at 1021-23. Under this infringement theory, the form of paroxetine discovered in the 1970s was, indeed, pure anhydrate; hemihydrate did not exist until late 1984.

> [SKB's expert] Dr. Bernstein testified that he was 'absolutely convinced' that no hemihydrate had existed before December 1984 . . . Dr. Terence Threlfall, Apo-

> tex's expert on polymorphism, testified [that] Dr. Bernstein's absolute certainty . . . is not tenable. No one knows when the hemihydrate form of paroxetine came into existence, although it is a reasonable inference that it did not exist in a detectable amount until then.

Id. at 1022. From that date forward, however, it was impossible to produce pure anhydrate in a "seeded" environment because even under normal climactic conditions, at least some of the anhydrate would "convert" to become hemihydrate.

> This process of 'seeding' the old with the new can be deliberate—that is, can be a method of manufacturing the new polymorph—or adventitious, a result of the fact that some of the crystals become airborne and 'contaminate' the laboratory or plant in which the old crystal is being manufactured. . . . [T]he seeds relevant to this case are seeds that cause one polymorph to convert to another and these seeds are crystals of the form to which conversion occurs. A single tiny crystal, constituting a single seed, might induce conversion. . . . The creation of the new polymorph is likely to make the laboratory or plant where it is produced seeded, with the result that efforts to produce the old polymorph may instead produce the new one, since it is the more stable form. In principle it should be possible to re-create the old polymorph, just by replicating the exact procedure by which it used to be created, only this time in a seed-free environment. . . . [I]n practice efforts to re-create old polymorphs do not always succeed, probably because the critical mass of molecules that is required to cause conversion is so minute. . . .

Id. at 1020. SKB therefore argues that any paroxetine manufactured in a seeded environment must inevitably contain at least some hemihydrate, that this condition has only prevailed

since some time in late 1984, and that Apotex's facilities have been or inevitably will become seeded.

> According to SmithKline, the BCI plant [in which Apotex manufactures anhydrate] is seeded with hemihydrate crystals because it was there that Apotex, exercising the broadened experimental-use privilege conferred by the Hatch-Waxman Act, used and made hemihydrate in the course of developing its anhydrous product.

Id. at 1024.

B. *Findings of Fact*

SKB's proof supporting this theory must rest upon factual demonstrations. As an appellate court, we accept all facts found by the district court unless they are clearly erroneous. *Shockley v. Arcan, Inc.*, 248 F.3d 1349, 1357 (Fed.Cir.2001). The district court, however, stated its most significant finding as an hypothesis:

> The conflicting testimony of Bernstein . . . on the one hand and of Threlfall on the other can largely be reconciled on the following hypothesis: while the presence of hemihydrate seeds in a batch of anhydrate is likely, provided the ambient humidity and temperature are no lower than is normal in the temperate zone, to produce conversion within a short time, once the amount converted reaches a few percent of the mixture further conversion is unlikely without substantially greater humidity, temperature, or pressure.

SK II, 247 F.Supp.2d at 1022-23. Findings of fact stated as hypotheses pose particularly challenging problems for appellate courts. Did the district court accept this hypothesis as a fact upon which legal arguments and conclusions can rest, or was the district court merely trying to make sense of the scientific testimony that the two experts proffered?

The district court's own legal conclusions make it clear that the court accepted them as facts, by stating, for example, that "[Apotex's] BCI plant *is* seeded as a result of the mid-1990s experiments," *id.* at 1032 (emphasis added), and that "the anhydrate as it proceeds through the process [at the BCI plant] will at several junctures be exposed to air that contains enough water molecules to permit conversion of anhydrate to hemihydrate." *Id.* These statements make sense *only* if the district court found that both seeding and conversion are valid scientific facts, at least as applied to paroxetine for the purposes of this case.

The district court's understandable hedging of its language when dealing with controversial scientific theories nevertheless led it to definitive factual conclusions: "BCI *probably* will be 'making' at least some hemihydrate crystals and therefore infringing, at least prima facie, patent '723 if claim 1 is interpreted to cover single crystals of the hemihydrate." *Id.* (emphasis added). "Some conversion from anhydrate to hemihydrate *is likely* to occur in a seeded facility in which the anhydrate is exposed to air; BCI's plant is seeded; and the anhydrate manufactured there is exposed to nondehumidified air before it leaves the plant." *Id.* (emphasis added). But in concrete syllogistic conclusion, "[t]his evidence *is sufficient to support an inference* that BCI will be making at least tiny amounts of the hemihydrate if it is permitted to manufacture the anhydrate." *Id.* (emphasis added).

The district court therefore found, as a matter of fact, that paroxetine anhydrate in a seeded environment characterized by normal climactic conditions *can* convert itself spontaneously into paroxetine hemihydrate. *Id.* The district court further found that SKB had met its burden of proving, by a preponderance of the evidence, that such conversion *was inevitable* at Apotex's BCI manufacturing facility. *Id.* at 1042-43.

The district court next turned to consider Apotex's defenses. "If . . . claim 1 is valid and will be infringed . . . by a single crystal of hemihydrate . . . [then] Apotex has a complete affirmative defense that SmithKline is the cause of the infringement." *Id.* at 1052. This conclusion makes sense only after a factual finding that Apotex's legal experimentation with Paxil[5] seeded the BCI plant. *Id.* at 1024. "Apotex cannot eliminate *all* crystals of hemihydrate; under a single-crystal interpretation of claim 1, [and] SmithKline is the sole cause of infringement." *Id.* at 1044 (emphasis in the original).

> Finally, the district court explained that it is difficult, and in some cases it may be impossible (paroxetine hydrochloride hemihydrate may be one of those cases—no one knows), to destroy all the seeds in seeded premises. . . . Dr. Bernstein testified that if Apotex, desperate to avoid a charge of infringement built a new plant in Antarctica where no hemihydrate seeds had ever been and started manufacturing anhydrate there, and a depressed worker in the plant dropped a Paxil on the floor, the result might be to seed the plant and make it impossible from then on to produce pure anhydrate there.

Id. at 1020-21.

In short, the district court made four critical factual findings: (1) Hemihydrate crystals did not exist before their first emergence in an SKB laboratory in late 1984, *id.* at 1025; (2) Hemihydrate seeds spread easily, and increasingly large parts of the environment are becoming seeded, *id.* at 1020-21; (3) Under normal climactic conditions in a seeded

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[5] Under the Hatch-Waxman Act, a generic drug manufacturer is allowed to experiment with a patented drug to prove that its planned product is bioequivalent to one already approved by the Food and Drug Administration (FDA). The district court viewed this statutory permission as an implied license, *SK II*, 247 F.Supp.2d at 1018, and attributed liability for the consequent seeding to SKB. *Id.* at 1044.

environment, at least some anhydrate crystals will convert spontaneously to become hemihydrate crystals, *id.* at 1022-23 and (4) Apotex's manufacturing facilities have been seeded, *id.* at 1024.

III.

A. *Public Notice*

These findings of fact highlight the unique challenge that the infringement analysis of the '723 Patent poses: infringing matter has an unusual tendency to "appear" even where it is unwanted. Such a spontaneous appearance of a patented product vitiates the public notice function of patents. *See id.* at 1028. Under normal circumstances,

> one of ordinary skill in the art should be able to read a patent, to discern which matter is disclosed and discussed in the written description, and to recognize which matter has been claimed. The ability to discern both what has been disclosed and what has been claimed is the essence of public notice. It tells the public which products or processes would infringe the patent and which would not.

PSC Computer Prods. v. Foxconn Int'l, 355 F.3d 1353, 1359 (Fed.Cir.2004). When the claimed product can be "made" via the spontaneous conversion of a noninfringing product into an infringing one, adequate notice is impossible—even if the claimed product was initially synthesized in a laboratory.

Long before 1952, when Section 112 formalized the modern written description requirement, the Supreme Court observed that:

> Whoever discovers that a certain useful result will be produced, in any art, machine, manufacture, or composition of matter, by the use of certain means, is entitled to a patent for it; provided he specifies the means he uses in a manner so full and exact, that any one

> skilled in the science to which it appertains, can, by using the means he specifies, without any addition to, or subtraction from them, produce precisely the result he describes. And if this cannot be done by the means he describes, the patent is void. And if it can be done, then the patent confers on him the exclusive right to use the means he specifies to produce the result or effect he describes, and nothing more.

O'Reilly v. Morse, 15 How. 62, 119, 14 L.Ed. 601 (1853). The Supreme Court further explained that

> [a]ccurate description of the invention is required by law, for several important purposes: 1. That the government may know what is granted, and what will become public property when the term of the monopoly expires. 2. That licensed persons desiring to practice the invention may know during the term how to make, construct, and use the invention. 3. That other inventors may know what part of the field of invention is unoccupied.

Bates v. Coe, 98 U.S. 31, 39, 25 L.Ed. 68 (1878). While these pre-1952 cases may not apply directly to the modern written description requirement of Section 112, they do demonstrate the longstanding centrality of the public notice function to patent policy.

Paroxetine hemihydrate forces us, for the first time, to confront the requirement that "a patentee specify in a manner so full and exact, that any one skilled in the science to which it appertains, can, by [*avoiding]* the means he specifies," *O'Reilly*, 15 How. at 119, 14 L.Ed. 601, *avoid producing the claimed product.* Otherwise, there will be no way for "other inventors [to] know what part of the field of invention is unoccupied." *Bates*, 98 U.S. at 39. Effective notice is impossible if a natural physical process can convert a non-infringing product into an infringing one.

The district court was correct in concluding that Claim 1 of the '723 patent, subject to the proper single crystal construction, fails to provide suitable notice. *SK II*, 247 F.Supp.2d at 1028, 1052. A paroxetine anhydrate manufacturer, such as Apotex, could exert reasonable efforts to manufacture only products already in the public domain, could direct its entire production process toward developing only products that scrupulously respected all patent rights, and could nevertheless infringe because a natural physical process acting upon its legitimate anhydrous product "made" new hemihydrous crystals that Apotex then "sold" to the public. "Apotex has tried to prevent conversion of its product to the patented form and a principal issue in this case is whether it has succeeded; there is no suggestion that Apotex *desires* conversion." *SK II*, 247 F.Supp.2d at 1015 (emphasis in original).

Were we to nevertheless hold Apotex liable as an infringer of Claim 1, we would effectively remove a valuable public-domain antidepressant, paroxetine anhydrate, from the market, and likely motivate potential inventors of superior grades of paroxetine to refocus their efforts elsewhere. This result is inconsistent with patent policy and—more importantly for the purposes of this court—it is incompatible with patent law. We would be holding valid a patent incapable of serving its important public notice function.

Claim 1 therefore cannot be held valid. But the failure of notice is a consequence of its invalidity, not the source of it. We must consider whether or not the '723 patent covers only patentable subject matter. *See Slawson*, 107 U.S. at 652, 2 S.Ct. 663.

B. *Patentable Subject Matter*

"Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent there-

fore . . ." 35 U.S.C. § 101. The Supreme Court has interpreted this statutory range of patentable subject matter to be quite broad, but hardly universal. "In choosing such expansive terms as 'manufacture' and 'composition of matter,' modified by the comprehensive 'any,' Congress plainly contemplated that the patent laws would be given wide scope." *Diamond v. Chakrabarty*, 447 U.S. 303, 308, 100 S.Ct. 2204, 65 L.Ed.2d 144 (1980). That wide scope nevertheless excludes laws of nature, natural phenomena, and abstract ideas. "Such discoveries are 'manifestations of . . . nature, free to all men and reserved exclusively to none.' " *Id.* at 309, 100 S.Ct. 2204, (quoting *Funk Bros. Seed Co. v. Kalo Inoculant Co.*, 333 U.S. 127, 130, 68 S.Ct. 440, 92 L.Ed. 588 (1948)). *See also Diamond v. Diehr*, 450 U.S. 175, 185, 101 S.Ct. 1048, 67 L.Ed.2d 155 (1981); *Parker v. Flook*, 437 U.S. 584, 589, 98 S.Ct. 2522, 57 L.Ed.2d 451 (1978).

"Phenomena of nature, though just discovered, mental processes, and abstract intellectual concepts are not patentable, as they are the basic tools of scientific and technological work." *Gottschalk v. Benson*, 409 U.S. 63, 67, 93 S.Ct. 253, 34 L.Ed.2d 273 (1972). A single standard applies to product claims and process claims alike. *Id.* "[W]hether patents are allowable for [challenged subject matter] is not a matter of discretion, but of law. . . . Either the subject matter falls within Section 101 or it does not." *Animal Legal Def. Fund v. Quigg*, 932 F.2d 920, 929-30 (Fed.Cir.1991). And as a matter of law, the critical distinction guiding all Section 101 inquiries into the patentability of subject matter is that human-made, or synthetic, products or processes are patentable, while products and processes of nature are not. *See Chakrabarty* at 313, 100 S.Ct. 2204; *J.E.M. AG Supply v. Pioneer Hi-Bred Int'l*, 534 U.S. 124, 130, 122 S.Ct. 593, 151 L.Ed.2d 508 (2001).

The district court found as a matter of fact that at some point, likely in late 1984, something occurred in SKB's

laboratories that gave rise to two new phenomena simultaneously. *SK II*, 247 F.Supp.2d at 1021-22. The first was a synthetic crystal later named paroxetine hemihydrate, *id.*, ostensibly a patentable human-made invention under *Chakrabarty*. The second was a natural physical process whereby paroxetine anhydrate (a pre-existing synthetic crystal that today is in the public domain) could, under normal climactic conditions and with no human intervention, bond with water molecules and convert itself into paroxetine hemihydrate, *SK II*, 247 F.Supp.2d at 1021-22, ostensibly an unpatentable, newly discovered natural process under *Chakrabarty*.

This distinction between the synthetic product and its natural "reproduction" process is subtle, but critical. Paroxetine hemihydrate is not the first invention to blur the line between a natural process and a synthetic product, nor is it the first to engender confusion in the patent law. In the Nineteenth Century, the conflation of the natural acoustical principles of telephony with the invention of telephone equipment gave rise to massive litigation. *See Telephone Cases*, 126 U.S. 1, 8 S.Ct. 778, 31 L.Ed. 863 (1888). In disentangling this complex patent litigation, the Supreme Court noted that:

> In one of the cases on appeal . . . the court says: "There can be no patent for a mere principle. The discoverer of a natural force or a scientific fact cannot have a patent for that." But it proceeds to make this exception nugatory by confounding the natural process (or scientific fact) with the invented process for working the apparatus; sustaining the patent for the last upon a construction which blindly sweeps in the first.

Id. at 270-71, 8 S.Ct. 778. The '723 patent similarly confounds the scientific fact of paroxetine conversion with the invented product of paroxetine hemihydrate—and SKB similarly asks us to "sustain[ ] the patent for the last upon a construction which blindly sweeps in the first." *Id.* We should

not only decline to do so, as the majority has and as the district court did in the alternative, but we should be clear about both the character and the implications of the underlying request.

Paroxetine hemihydrate is presumably a synthetic compound, created by humans in a laboratory, never before existing in nature, that is nevertheless capable of "reproducing" itself through a natural process. *SK II*, 247 F.Supp.2d at 1022-23. This crystalline compound raises a question similar to one that might arise when considering the invention of a fertile plant or a genetically engineered organism, capable of reproduction, released into the wild. Consider, for example, what might happen if the wind blew fertile, genetically modified blue corn protected by a patent, from the field of a single farmer into neighboring cornfields. The harvest from those fields would soon contain at least some patented blue corn mixed in with the traditional public domain yellow corn—thereby infringing the patent. The wind would continue to blow, and the patented crops would spread throughout the continent, thereby turning most (if not all) North American corn farmers into unintentional, yet inevitable, infringers.[6] The implication—that the patent owner would be entitled to collect royalties from every farmer whose cornfields contained even a few patented blue stalks—cannot possibly be correct. The underlying question that engaged the district court, and that led it to develop numerous alternative holdings, is *why* this implication is incorrect.

At oral argument, when faced with this hypothetical, SKB expressed its belief that such a blue-corn patent would be "very strong." Such a belief is misplaced. The implicit

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[6] Although intent is not a factor in determining infringement, public notice is required as a predicate to the validity of a patent. *Jurgens v. CBK, Ltd.*, 80 F.3d 1566, 1570 n. 2 (Fed.Cir.1996). The hypothetical causes unavoidable infringement even in situations where the public would, in good faith, want to avoid infringing.

concept of "inevitable infringement" stems from the inevitable failure of the patent to provide public notice—which, in turn, stems from the inherently unpatentable nature of the claimed subject matter.

This Section 101 problem therefore brings us full circle, back to the impossibility of public notice. Under normal circumstances, inventors other than the patentee will understand how to avoid infringing a patent by avoiding the claimed product. Because products, such as our hypothetical blue corn or SKB's paroxetine hemihydrate, that can be "made" through a natural process of spontaneous conversion imply inevitable infringement, no combination of claim language and written description could possibly teach even one skilled in the art how to avoid infringement. It is unsurprising that a requirement considered so trivial for most patentable products that we are content to let it remain implicit, namely a lesson in infringement avoidance, is effectively impossible for subject matter unpatentable under Section 101. In short, patent claims drawn broadly enough to encompass products that spread, appear, and "reproduce" through natural processes cover subject matter unpatentable under Section 101—and are therefore invalid.

C. *Invalidity*

Technological advances have forced this court, our predecessor court, and the Supreme Court to consider the line between the natural and the non-natural—including such inventions as non-naturally occurring plants and bacteria—several times over the past few decades. *See, e.g., In re Bergy*, 596 F.2d 952 (CCPA 1979), *rev'd sub nom Diamond v. Chakrabarty*, 447 U.S. 303, 100 S.Ct. 2204, 65 L.Ed.2d 144 (1980); *Pioneer Hi-Bred Intl, Inc. v. J.E.M. Agric. Supply, Inc.*, 200 F.3d 1374 (Fed.Cir.2000), *affd.* 534 U.S. 124, 122 S.Ct. 593, 151 L.Ed.2d 508 (2001). Paroxetine hemihydrate now appears to be the first patent litigated that forces the courts to consider the patentability of prod-

ucts and/or processes launched in a laboratory and released into nature.

Despite the complexity of the issue, the analysis is straightforward. An invention synthesized for the first time in a laboratory is eligible for patent protection under Section 101. Processes for producing this synthetic product in the laboratory and/or for using this synthetic product may also be eligible for patent protection under Section 101. However, a natural reproduction process, whether sexual, asexual, part of a chain reaction, or a process of decay, is ineligible for patent protection under Section 101. *Chakrabarty*, 447 U.S. at 309, 100 S.Ct. 2204; *Funk Bros.*, 333 U.S. at 130, 68 S.Ct. 440. An item reproduced by such a natural process, whether an inorganic structure or a life form, must ipso facto be ineligible for patent protection under Section 101.

The Supreme Court has cited with approval the Congressional Record surrounding the adoption of the Plant Patent Act of 1930:

> [A] plant discovery resulting from cultivation is unique, isolated, and is not repeated by nature, *nor can it be reproduced by nature unaided by man*. . . ." S.Rep. No. 315, supra, at 6; H.R.Rep. No. 1129, supra, at 7. Congress thus recognized that the relevant distinction was not between living and inanimate things, but between products of nature, whether living or not, and human-made inventions.

Chakrabarty, 447 U.S. 303, 100 S.Ct. 2204, 65 L.Ed.2d 144 (emphasis added). In its recent ruling confirming that hybrid plants are patentable subject matter under Section 101, the Supreme Court noted that "[h]ybrid plants . . . generally do not reproduce true-to-type, i.e., seeds produced by a hybrid plant do not reliably yield plants with the same hybrid characteristics. Thus, a farmer who wishes to continue

growing hybrid plants generally needs to buy more hybrid seed." *J.E.M.*, 534 U.S. at 128, 122 S.Ct. 593.

The principle unifying these statements about patentability made in 1930, 1980, and 2001 is that products capable of being "reproduced by nature unaided by man," *Chakrabarty*, 447 U.S. 303, 100 S.Ct. 2204, are not patentable subject matter under Section 101. Though the parties have not briefed this question directly, they and the district court have provided more than sufficient facts to obtain a dispositive and incontrovertible legal determination that Claim 1 of the '723 Patent is invalid under Section 101.

The '723 patent, correctly construed, claims every single crystal of paroxetine hemihydrate, including those crystals arising through natural conversion. The district court properly admitted SKB's proffered expert testimony about the scientific mechanism underlying natural conversion, *SK II*, 247 F.Supp.2d at 1019-20, under *Daubert v. Merrell Dow Pharmaceuticals*, 509 U.S. 579, 113 S.Ct. 2786, 125 L.Ed.2d 469 (1993), and *General Electric v. Joiner*, 522 U.S. 136, 118 S.Ct. 512, 139 L.Ed.2d 508 (1997) , weighed it in conjunction with contradictory testimony proffered by Apotex's experts, *SK II*, 247 F.Supp.2d at 1022, and concluded that at least some of Apotex's anhydrate would convert itself to hemihydrate. *SK II*, 247 F.Supp.2d at 1022-23.

These findings lead to an inescapable conclusion—a conclusion that the majority attempts to dismiss as a question of "scope," rather than of patentability. Had SKB claimed "*synthetic* or *non-naturally occurring* crystalline paroxetine hydrochloride hemihydrate," the claim would have covered only patentable subject matter, and Apotex would be entitled to a judgment of noninfringement. Had SKB explicitly claimed the crystals converted in Apotex's facilities, as either "the *natural process* of converting paroxetine anhydrate to paroxetine hemihydrate" or "crystalline paroxetine hydrochloride hemihydrate *arising through natural conversion*,"

unpatentability under Section 101 would be manifest; though the claimed matter would be a useful composition, it would be one that occurred in nature. *See Chakrabarty*, 447 U.S. at 309, 100 S.Ct. 2204; *Funk Bros.*, 333 U.S. at 130, 68 S.Ct. 440. By claiming simply "crystalline paroxetine hydrochloride hemihydrate" with no reference to how it was produced, SKB effectively claimed "crystalline paroxetine hydrochloride hemihydrate *whether non-naturally occurring or arising through natural conversion*." Claim 1, as issued, therefore combines patentable and unpatentable subject matter, and is invalid under Section 101. The "confusion" to which the majority alludes should never arise because we cannot reach Section 102 unless the claimed matter can overcome the hurdle of Section 101.

Inventors wishing to claim products that can either be synthesized in laboratories or generated by natural processes may protect themselves by incorporating negative limitation terms like "non-natural" or "non-human" into the claims that they submit for examination. *See Amgen Inc. v. Hoechst Marion Roussel*, 314 F.3d 1313, 1329 (Fed.Cir.2003); *Animal Legal Def. Fund*, 932 F.2d at 923; *In re Wakefield*, 422 F.2d at 904. SKB made no such distinction. SKB, despite an early recognition of seeding and conversion, *SK II*, 247 F.Supp.2d at 1022, claimed all paroxetine hemihydrate crystals, including both those "born" of natural conversion without human intervention and those "made" in a laboratory through explicit human effort. SKB further demonstrated its claim to a possessory right in naturally occurring crystals by pursuing this litigation, and articulated this claim explicitly during oral argument.

IV.

The asserted breadth of Claim 1 makes sense only under the erroneous belief that patents may protect products spread and reproduced by natural processes, directly contradicting our well established understanding of the limits imposed by

Section 101. Given current scientific trends, such a belief could easily lead to misdirected research investments, to inappropriately issued patents, and to a widespread in terrorem effect crippling entire industries whose artisans learn that even their best efforts to respect patent rights may not save them from liability as inadvertent, inevitable infringers. As the district court recognized, the notice function of patents is meaningless in such an environment, *SK II*, 247 F.Supp.2d at 1028. The lack of suitable notice could easily chill innovation, inquiry, experimentation, and commercial development.

Though the majority's approach to invalidating Claim 1 of the '723 patent under Section 102(b) defuses these negative consequences with respect to paroxetine, it does so at the cost of creating unfortunate precedent that will complicate future considerations of the experimental use doctrine. It also fails to address the central anomaly that the district court identified. We do no one any favors by allowing this important question to remain open. We should announce, as a court, that the patent law does not sanction the concept of inevitable infringement—lest someone mistakenly believe that it does.

I would hold that because SKB's assertion of the single crystal theory provides the correct construction of Claim 1, the '723 patent claims paroxetine hemihydrate crystals reproduced by nature unaided by man—unpatentable subject matter—and is therefore invalid under 35 U.S.C. § 101.

APPENDIX D

UNITED STATES DISTRICT COURT
N.D. ILLINOIS
EASTERN DIVISION

No. 98 C 3952

SMITHKLINE BEECHAM CORP.
and Beecham Group, P.L.C.,
Plaintiffs,

v.

APOTEX CORP., Apotex, Inc., and TorPharm, Inc.,
Defendants.

March 3, 2003

OPINION

RICHARD A. POSNER, *Circuit Judge*.

I conducted a bench trial in this patent infringement case between February 5 and 21 of this year, by designation of the chief circuit judge pursuant to 28 U.S.C. § 291(b), and this opinion comprises the findings of fact and conclusions of law that Fed.R.Civ.P. 52(a) requires me to issue. The plaintiffs in their post-trial brief erroneously refer to "findings" that I made in the course of the trial. I made no findings during the trial; these are my findings.

The Procedural Setting and Pretrial Rulings

The plaintiffs are two subsidiaries of Glaxo, the British manufacturer of pharmaceutical drugs. I shall refer to the two collectively as "SmithKline". The defendants are Apotex, Inc., a Canadian manufacturer of generic pharmaceuticals, and affiliates of it; I shall refer to the defendants collectively as "Apotex." SmithKline claims that Apotex is (more pre-

cisely, as I'll explain in due course, will be) infringing SmithKline's U.S. patent 4,721,723, or "723" as the parties refer to it, after its last three digits. The patent is on an antidepressant drug that SmithKline sells under the trade name Paxil. Paxil is now the leading brand of antidepressant drug, with annual sales of $3.2 billion worldwide, about two-thirds in the United States.

SmithKline argues not only that Apotex is an infringer but also that the infringement is willful, entitling SmithKline to additional relief, namely an award of attorneys' fees. Apotex contends that the patent (more precisely, the claim in the patent that covers the composition of the drug, as distinct from claims concerning processes for making the drug) is invalid but, if valid, not infringed, and if valid and infringed still not infringed willfully. I deferred consideration of the issue of willfulness to such time as I might hold the patent valid and infringed. Since I hold that the patent although valid is not infringed and further that even if it is valid and infringed SmithKline is entitled to no relief, I do not reach the issue of willfulness. Should the case be remanded to me, I would have to conduct a further evidentiary hearing in order to resolve that issue.

Judge (now Chief Judge) Kocoras of the Northern District of Illinois, to whom the case was initially assigned when it was filed back in 1998, made a number of pretrial rulings, and I must consider the extent to which I am bound by them in accordance with the doctrine of law of the case. The doctrine requires a court to adhere to its previous rulings in the same litigation unless there is a compelling reason, such as an intervening change of law or newly discovered evidence, to reexamine them. Its usual application is to a case that is remanded by the court of appeals and then returns to that court by an appeal from the decision on remand. The doctrine counsels the court not to revisit the issues it decided on the first appeal, but it does not limit a trial judge's changes

of mind during the course of a litigation uninterrupted by an appeal, and such changes of mind are of course frequent. When however the judges in a case are switched in midstream, as happened here, the successor judge may not reconsider his predecessor's rulings with the same freedom that he may reconsider his own rulings. "As this court [the Seventh Circuit] explained in *Williams v. C.I.R.*, 1 F.3d 502 (7th Cir.1993), the law of the case doctrine in these circumstances reflects the rightful expectation of litigants that a change of judges midway through a case will not mean going back to square one. See also *Christianson v. Colt Industries Operating Corp.*, 486 U.S. 800, 816-17, 108 S.Ct. 2166, 100 L.Ed.2d 811 (1988). Although the second judge may alter previous rulings if he is convinced they are incorrect, 'he is not free to do so . . . merely because he has a different view of the law or facts from the first judge.' *Williams*, 1 F.3d at 503. Instead, the presumption is that earlier rulings will stand, even though it can be overcome for compelling reasons (such as new controlling law or clear error)." *Best v. Shell Oil Co.*, 107 F.3d 544, 546 (7th Cir.1997); see also *Peterson v. Lindner*, 765 F.2d 698, 704 (7th Cir.1985); *Fagan v. City of Vineland*, 22 F.3d 1283, 1290 (3d Cir.1994).

The reader may wonder at my citing Seventh Circuit rather than Federal Circuit cases on this point, since if my decision is appealed it will be appealed to the Federal Circuit. But that court applies the law of the circuit in which the district court is located to procedural matters that are not unique either to patent law or to appellate as distinct from trial procedure. See *Panduit Corp. v. All States Plastic Mfg. Co.*, 744 F.2d 1564, 1574-75 (Fed.Cir.1984) (per curiam); *Biodex Corp. v. Loredan Biomedical, Inc.*, 946 F.2d 850, 858 (Fed.Cir.1991). The doctrine of law of the case is not unique in either sense and so its application here is governed by Seventh Circuit (and of course Supreme Court) precedent.

The parties asked me to reexamine several of Judge Kocoras's rulings, but only one met the criteria for reexamination, his order of July 16, 2002. That order excluded evidence that infringement of SmithKline's patent 723 would occur when Apotex's product combined with the fluids in a patient's stomach to create small amounts of the patented product, or perhaps even earlier when the patient opened the bottle of tablets and took out a pill, reexposing it as well as the remaining pills in the bottle to air and hence to moisture. The patient would be the infringer in either of those cases (assuming that there is any infringer in those cases, which I express no view on), but SmithKline argues that Apotex, knowing that infringement would occur, would be guilty of inducement to infringe. 35 U.S.C. § 271(b). As it pointed out in its motion to vacate the July 16 order, the Federal Circuit's decision in *Warner-Lambert Co. v. Apotex Corp.*, 316 F.3d 1348 (Fed.Cir.2003), undercuts the ground of that order and so reexamination is warranted. But *Warner-Lambert* also makes clear that the burden of proving inducement is a heavy one, *id.* at 1363-64, and SmithKline's motion provided no ground for thinking that SmithKline could carry the burden. Even if a patient's gastrointestinal juices convert the nonpatented product that Apotex plans to manufacture to the product patented by SmithKline and Apotex knows this will happen, there is no evidence that Apotex intends, in the sense of desires or is working to achieve, this result. For the gastrointestinal "infringement" does nothing for Apotex commercially; it merely increases Apotex's exposure to liability. That is equally true if infringement is thought to occur when the bottle is opened. Apotex has tried to prevent conversion of its product to the patented form and a principal issue in this case is whether it has succeeded; there is no suggestion that Apotex *desires* conversion. I therefore denied the motion to vacate the July 16 order and I adhere to that ruling. But I add that, in light of the discussion of relief in the last part of this opinion, it is

plain that if Apotex were guilty of inducement in the circumstances outlined above, SmithKline would not be entitled to any relief.

The Background of the Case

Early in 1977 a British company called Ferrosan obtained a U.S. patent ("196," also known as the Christensen patent) on a set of compounds that included what came to be called "paroxetine." The paroxetine molecule consists of carbon, nitrogen, oxygen, hydrogen, and fluorine atoms arranged in a particular configuration. When combined with additional atoms to form a salt molecule (a hydrochloride, for example, if paroxetine base is bathed in hydrochloric acid), and mixed with additional compounds (binders, lubricants, disintegrants, etc.—collectively, "excipients") to bulk up into a pill and to improve handling, tableting, and dissolution, paroxetine was believed, correctly as it turned out, to be effective in treating depression and related psychiatric disorders. Like fluoxetine—the active ingredient in Prozac—paroxetine is a selective serotonin reuptake inhibitor, which helps to assure an adequate supply of the "feel good" enzyme serotinin to brain cells. Although mention of Prozac is a reminder that Paxil faces competition from other SSRIs (not to mention other types of antidepressant drug, and other modes of treatment altogether), there are medically significant differences, both in efficacy and side effects, even among the different SSRIs. Paxil, for example, is preferred to Prozac by many doctors for the treatment of depression coupled with anxiety (a common combination), because unlike Prozac it has been approved by the Food and Drug Administration for anxiety disorders.

Ferrosan was not a manufacturer of pharmaceutical drugs, so in 1980 it licensed its paroxetine patent to SmithKline. Although the patent specified paroxetine maleate as the paroxetine salt it was claiming, Ferrosan had already, after some travail, succeeded in creating a paroxetine hydrochloride in crystalline form, hydrochloride being a preferred

salt for pharmaceutical purposes. In 1981 SmithKline began manufacturing paroxetine hydrochloride in its Harlow (U.K.) plant.

Before a pharmaceutical drug can be placed on the market, it must undergo elaborate testing for safety and efficacy, and so quantities of paroxetine hydrochloride were distributed to different parts of the world, including the United States, for use in clinical trials. SmithKline has a laboratory in Worthing, England, and samples of paroxetine hydrochloride were sent there in bulk form—that is, before being made into pills—to be used in experiments on improving the production of the bulk material. In March 1985, a chemist at Worthing, Alan Curzons, experimenting on ways to produce paroxetine hydrochloride, discovered that he had created a new form of the compound, which he dubbed "Form 1" to distinguish it from the anhydrous form, which he dubbed (confusingly, because it was the earlier form) Form 2. Tests that Curzons performed confirmed that Form 1 was indeed a distinct crystalline form of paroxetine hydrochloride.

Crystallinity is central to this case. When molecules are bound together, by interatomic forces that radiate beyond the "boundaries" of the molecules themselves, in a definite structure which is then repeated over and over again without significant change, the agglomerations that result are called "crystals." (These and other relevant aspects of crystallography are lucidly discussed in Stephen R. Byrn, Ralph R. Pfeiffer & Joseph G. Stowell, *Solid-State Chemistry of Drugs* (2d ed.1999). See especially Chapters 1, 10-11, and 13. Dr. Byrn testified for SmithKline at the trial.) The molecules are like the intersections of the slats of a lattice; the slats correspond to the forces that hold the molecules in their fixed positions, and the multiplication of the lattice is the crystal. The crystal's minimum structure—the structure that, repeated, constitutes the crystal—is called the "unit crystal cell." The unit crystal cell is not itself a crystal, however.

That is by definition: a crystal is a multiple of the structure that defines the unit crystal cell. Moreover, were there only, say, two unit crystal cells, the molecules composing them would not crystallize because the interatomic forces would be too weak to maintain the structure. The number of unit crystal cells required to create the minimum crystal is very small, however: depending on the molecules and the structure, as few as ten molecules may be enough to create an actual crystal. Stated differently, a large crystal might in principle though not in practice be cut into an immense number of utterly minute crystals.

The same substance will sometimes appear in more than one crystalline form—will be, that is, "polymorphous." The molecules are the same but the lattice is different. The difference can affect the melting point of the crystal (the point at which the crystal structure is destroyed by heat, rendering the substance liquid) and other properties of the crystal, such as hardness: a dramatic example is graphite and diamonds, both of which are crystals of carbon. Because a different arrangement of molecules implies a different pattern of bonds, and different bonds vibrate at different frequencies, different polymorphs of the same chemical produce different x-ray diffraction patterns and infrared spectra, which are two types of graphic mapping of the atomic forces binding the crystal.

The form of paroxetine hydrochloride that Curzons discovered was not a true polymorph, although often and loosely referred to as such, as I shall do; rather, it was a "pseudopolymorph." These critters not only have their molecules arranged differently but also have a slightly different molecular composition. A common type of pseudopolymorph is a *solvate*, which is a crystal in which molecules of a solvent, such as water, have become "caught" inside the crystal and have bonded with the other molecules in an altered crystalline structure. When the trapped and bonded solvent is water, the solvate is called a *hydrate*. And when it

is a hydrate in which there is one water molecule for every two of the other molecules constituting the unit crystal cell, in this case molecules of paroxetine hydrochloride, the hydrate is called a *hemihydrate*. Despite the presence of water molecules, a hemihydrate is a solid, a powder, at room temperature.

At the time that Curzons had his eureka moment, Smith-Kline's plant at Harlow was producing only a paroxetine hydrochloride anhydrate (at least as far as it knew), which is to say a crystalline form of paroxetine that does not contain a bound water molecule. (This anhydrate is what Curzons dubbed "Form 2.") Curzons made a batch of paroxetine, added isopropyl alcohol, a solvent, and found that the batch crystallized as a hemihydrate rather than as an anhydrate. And here an oddity, as it strikes a lay observer at any rate, should be noted. The anhydrous form of crystalline paroxetine hydrochloride is hygroscopic; that is, it attracts water, perhaps because of the position of the fluorine atoms in the anhydrous form, though this was merely a speculation by one of the expert witnesses. The water it attracts either sits on the outside of the paroxetine molecule, loosely attached and therefore easily dispersed by heating at a significantly lower temperature than required to liberate the bound water molecule from the hemihydrate, or, if it has found its way inside the crystal, it is nevertheless again readily dispersed, because it is not held to the paroxetine molecules by strong interatomic bonds. In contrast, the hemihydrate is not hygroscopic because it is not "thirsty" —it has already drunk, as it were.

The anhydrate's hygroscopicity makes it difficult to handle in the manufacturing process; measures must be taken to control humidity and other sources of moisture lest the anhydrate become so "soggy" that it degrades into other compounds, which might impair the safety or efficacy of the product. So when Curzons realized that he had obtained a

hemihydrate he immediately grasped the potential commercial significance—and also and distinctly the potential *patent* significance, which has now to be explained—of his discovery.

Because it takes a long time for a new drug to be approved by the U.S. Food and Drug Administration for sale to the American public, the actual period during which the producer has an exclusive right to make, use, and sell the drug is shorter than the statutory term of the patent. In the case of patent 723 for example, the patent at issue in this case, the application was filed in 1985 and granted in 1988, and the patent expires in 2006; but because the FDA process delayed the commencement of commercial sale to 1993 (FDA approval having been obtained the previous year), the effective term of the patent has been compressed to 13 years. Indeed, were it not for 35 U.S.C. § 156(c), a provision added to the patent statute by the Hatch-Waxman Act (the Drug Price Competition and Patent Term Restoration Act of 1984, Pub.L. No. 98-417, 98 Stat. 1585 (1984)), SmithKline would have had only 12 years of effective patent protection, because, were it not for that provision, patent 723 would expire in 2005—20 years after the date of application and 17 years after the date the patent was issued—rather than in 2006.

The compression of the commercially significant patent term by reason of the regulatory process at the FDA is a matter of concern to the manufacturers of new drugs. The cost of developing such a drug is often very great, in part because attempts to develop a new drug that will be both safe and effective often fail and the cost of these "dry holes" must be reckoned into the cost of the drugs that succeed, as it is only out of the revenues of those drugs that the costs of the dry holes can be recovered. The greater the upfront cost of developing a product, the more time is required to recoup the cost and so (other things being equal) the longer is the socially optimal patent term. The costs incurred in running the gauntlet of FDA approval not only increase the manu-

facturer's upfront development cost but compound the effect of the delay, also due largely to the FDA, between obtaining a patent and actually being able to market the patented drug to the consuming public. Although Ferrosan obtained its patent on paroxetine in 1977, the product still had not come to market as of 1985, when it was superseded in SmithKline's patent planning by the hemihydrate discovered that year.

Until the Hatch-Waxman Act was passed in 1984, the costs and delays imposed by the FDA's procedures worked in favor of as well as against the manufacturers of patentable drugs. The reason is that generic manufacturers (such as Apotex), that is, manufacturers of drugs that have come off patent, either because the patent has been invalidated or, more commonly, because the patent has expired, also have to obtain the FDA's approval before they can sell the generic drug in the United States. And, before Hatch-Waxman, the generic manufacturer could not, in demonstrating to the FDA that his generic version would be no less safe and effective than the patented original, rely on the animal and human tests conducted by the manufacturer of the patented drug. He had to do his own tests. This required him to make or use the patented product, but he could not do so lawfully before the drug came off patent unless he had a license from the patentee—otherwise he would be an infringer because the Federal Circuit had held that the "experimental use" defense to patent infringement was inapplicable to experiments having commercial aims. *Roche Products, Inc. v. Bolar Pharmaceutical Co.*, 733 F.2d 858, 863 (Fed.Cir.1984). The upshot was that the generic manufacturer could not begin the process of seeking FDA approval until the patent expired, and given the length of that process the practical effect was to extend the period of patent protection well beyond the statutory term. The Hatch-Waxman Act shortened the process both by allowing the generic companies to take a free ride on the results of the patentee's safety and efficacy testing so long as they could show that their product was bioequivalent to the

original and by allowing them to make and use the patented product, even though the patent hadn't yet expired, in order to demonstrate bioequivalence.

This case differs from the standard case to which Hatch-Waxman applies because Apotex claims to be making a drug that while bioequivalent to a patented drug does not infringe the patent because it is a different compound. Apotex still had to convince the FDA of this bioequivalence, and whether to aid in demonstrating this or (more likely) merely to learn more about the production of paroxetine, Apotex bought some Paxil tablets, extracted the hemihydrate from them, and even made its own hemihydrate. Although this experimentation amounted to a making or use (in fact both) of the patented hemihydrate, SmithKline concedes that it was not infringement because it fell within the expanded experimental-use privilege created by the Hatch-Waxman Act.

The Act allows the generic manufacturer to file an Abbreviated New Drug Application (ANDA)—abbreviated because the applicant has only to demonstrate bioequivalence, and not safety and efficacy as an original matter—*before* the patent expires on the drug that it wants to produce and sell, though it may not begin to sell the drug until the patent either expires or is declared invalid. If the manufacturer wants to sell its generic equivalent before expiration of the patent, on the ground that the patent either is invalid or won't be infringed because while the two drugs are bioequivalent they are not the same invention, he has to so state in his ANDA. The Act authorizes the patentee in such a case, if he doesn't agree that the patent is invalid or even if valid will not be infringed, to sue the generic manufacturer for infringement, even though there is no infringement in the usual sense because the generic manufacturer has not yet begun to make (other than for permitted experimental purposes) or sell his knock-off of the patented drug.

Had the Act stopped there, its unequivocal effect would have been to shorten the economically significant patent term of drugs. But as a concession to the manufacturers of patented drugs, who had complained with much support in the academic literature about the length of time it took to get a new drug approved by the FDA, Congress tolled the date of expiration of drug patents (the patent term for all utility patents, including therefore drug patents, was then 17 years but in 1995 it was increased to 20 years) during the period in which an application for a new drug was under regulatory review. The Act capped the extension for patents such as 723 issued after the Act was passed at five years. 35 U.S.C. § 156(g)(6)(A). And patent protection could not extend beyond 14 years after the FDA had approved the new-drug application. 35 U.S.C. § 156(c)(3).

The manufacturers of patented drugs were not happy about the trade, in part at least for a reason that the facts of the present case illuminate. The Ferrosan patent (patent 196) expired in 1992. Yet as I have pointed out, as late as 1984, with only eight years to expiration, paroxetine made under that patent had not yet been placed on the market. If, however, the hemihydrate version of the molecule could be patented, the effect might be a considerable extension in the effective patent term of paroxetine because it might become difficult or even impossible to manufacture the pure anhydrous form after the Ferrosan patent expired.

How so? Dr. Joel Bernstein, one of SmithKline's expert witnesses at the trial, is an authority on "disappearing polymorphs." See Joel Bernstein, *Polymorphism in Molecular Crystals* 89-92 (2002); J.D. Dunitz & J. Bernstein, "Disappearing Polymorphs," 28 *Accounts of Chem. Res.* 193 (1995); see also Byrn, Pfeiffer & Stowell, *supra*, at 463. The term refers to the fact that after a new polymorph or pseudopolymorph appears, the process that had been used to make the old polymorph may no longer produce it—may

produce instead the new one. Actually there's an ambiguity buried in this formulation that is important to this case. A polymorph could disappear in the literal sense that it could no longer be created; or it could disappear in the more limited sense that the *pure* form of the old polymorph could no longer be created—the new polymorph would be an indelible though possibly minor and functionally inert component of any batch of the old.

The causal mechanism of polymorphic creation and transformation is not clear—polymorphism simply is not well understood by science, because of the complexity of the atomic interactions that produce it—but it seems to involve the confluence of three factors. First, according to Ostwald's Rule, a well-attested scientific principle, later-appearing polymorphs tend to be more stable than the earlier ones. If there is metamorphosis (interconversion, chemists call it), it tends naturally to be in the direction of more stable forms. A more stable form is less likely to change into a less stable one than vice versa, and so there is a drift toward the more stable polymorphs.

Second, impurities retard crystallization, including crystallization in new forms, and the progress of technology has yielded a secular decline in the proportion of impurities in manufactured products. And third, once a new and more stable crystal emerges, should it be mixed, even in very small quantities, with the old, less stable crystal, the old form may convert to the new. This process of "seeding" the old with the new can be deliberate—that is, can be a method of manufacturing the new polymorph—or adventitious, a result of the fact that some of the crystals become airborne and "contaminate" the laboratory or plant in which the old crystal is being manufactured.

I must pause over the terms "seed" and "seeding" because of the importance they assumed in the trial. In its broadest crystallographic sense a seed is any bit of matter that

precipitates crystallization; it could be a grain of dust. But the seeds relevant to this case are seeds that cause one polymorph to convert to another and these seeds are crystals of the form to which conversion occurs. See Bernstein, *supra,* at 90-91. A single tiny crystal, constituting a single seed, might induce conversion. *Id.* at 91.

The first two factors that I have discussed under the rubric of "disappearing polymorphs" together provide the most persuasive explanation for the initial appearance of a new polymorph, while the first and third provide the most persuasive explanation for the "disappearing polymorphs" phenomenon itself. The creation of the new polymorph is likely to make the laboratory or plant where it is produced seeded, with the result that efforts to produce the old polymorph may instead produce the new one, since it is the more stable form. In principle it should be possible to re-create the old polymorph, just by replicating the exact procedure by which it used to be created, only this time in a seed-free environment. Although it is difficult, and in some cases it may be impossible (paroxetine hydrochloride hemihydrate may be one of those cases—no one knows), to destroy all the seeds in seeded premises, crystalline seeds, unlike the pods in *Invasion of the Body Snatchers*, do not traverse galactic distances under their own power. Unless they are carried in samples or on a person's clothing from one seeded premises to another, the new premises will not be seeded and so it should be possible to re-create the old polymorph there. But this, as Dr. Bernstein explained, is in principle; and in practice efforts to re-create old polymorphs do not always succeed, probably because the critical mass of molecules that is required to cause conversion is so minute. In his book, Dr. Bernstein suggests that "a few tens of molecules" may be the minimum for conversion. Bernstein, *supra*, at 91. He was writing about polymorphs in general rather than about paroxetine, but it was implicit in Bernstein's testimony and also that of Dr. Byrn, and not persuasively

countered by Apotex's expert witnesses, that the critical mass of paroxetine hydrochloride hemihydrate crystals required to induce conversion in a batch of anhydrous paroxetine is probably of the same order of magnitude (or minitude). Even if a seed required not ten but ten million molecules, a particle at the limit of visual detection would contain enough paroxetine hydrochloride hemihydrate to make more than one hundred million seeds. And there is no method of ventilation or fumigation that will eliminate all the hemihydrate crystals from a manufacturing environment.

Dr. Bernstein testified that if Apotex, desperate to avoid a charge of infringement, built a new plant in Antarctica where no hemihydrate seeds had ever been and started manufacturing anhydrate there, and a depressed worker in the plant dropped a Paxil on the floor, the result might be to seed the plant and make it impossible from then on to produce pure anhydrate there. For that matter, he might have dropped it on the floor of his bathroom at home, releasing crystals that adhered to his skin or clothing. Bernstein described a remarkable episode involving the AIDS drug ritonavir, another polymorphic crystal. See also Sanjay R. Chemburkar *et al.*, "Dealing with the Impact of Ritonavir Polymorphs on the Late Stages of Bulk Drug Process Development," 4 *Organic Process Res. & Dev.* 413 (2000). Abbott began commercial production of the drug in 1996. Two years later a previously unknown—and, characteristically, a more stable—polymorph (Form II) appeared in the plant in the United States in which the final product was being manufactured. Immediately the old polymorph (Form I) began converting to the new. This precipitated a "market crisis," *id.* at 413, because unlike anhydrous and hemihydrous paroxetine crystals, Form I and Form II ritonavir were not bioequivalent. Fortunately (or so it seemed), Form II (the new polymorph) had not yet been observed in the plant in Italy where the bulk ritonavir was produced—but shortly after a visit to that plant by scientists who had been exposed to Form II, Form II showed up there

too, probably (Bernstein omitted the qualification) as a result of seeding from Form II crystals on the scientists' clothing. Eventually Abbott was able to produce a version of Form I that would not convert—entirely; but the new version did contain up to 3 percent of Form II. *Id.* at 417.

Because the mechanism of seeding—the process, occurring at the atomic level, by which contact between the more and the less stable polymorph causes the latter to convert to the former—has not yet been discovered, Apotex argues that there is no scientific basis for believing that seeding occurs. But this is obviously wrong. Many scientific phenomena are identified before their causal mechanism is understood. Newton was distressed that he could not identify the causal mechanism behind the law of universal gravitation, which he had discovered, because according to that law bodies at a distance, with no intermediate links, were exerting force on each other.

Seeding appears to have been at work in Alan Curzons' laboratory. One might have supposed that the unexpected result of his experiment had been produced by the exact combination of steps that he had taken in the making and crystallizing of paroxetine, including the choice of solvent to precipitate crystallization. But no; he soon discovered that it was very easy, using a variety of solvents, to produce hemihydrate—and the likeliest explanation is that the first batch of hemihydrate that he created had seeded his lab.

This leaves unexplained, however, why his initial experiment resulted in hemihydrate. Remember that he was not trying to produce a hemihydrate; the result of the experiment was serendipitous. One possibility is that as a result of the progress of technology, whereby as I noted, over time the proportion of impurities in manufactured products diminishes, the chemical mixture on which he performed his experiment was so far free from impurities that the same application of solvent that had previously produced only

anhydrous crystals now produced hemihydrous ones. Another possibility is that batches of paroxetine shipped from Harlow to Worthing had already seeded Curzons' lab because the manufacturing process at Harlow had, though without anyone's knowing it, already produced hemihydrate. For, once alerted by the outcome of Curzons' experiment to the existence of the hemihydrate, SmithKline discovered that a batch of paroxetine produced at Harlow in December 1984 (HP 23) and another batch produced there in the following month (HP 24) had both been hemihydrate. As SmithKline states in its post-trial brief, "no one knows for sure" how these early batches (including Curzons') "came to be crystalline paroxetine hydrochloride hemihydrate."

Nevertheless Dr. Bernstein testified that he was "absolutely convinced" that no hemihydrate had existed before December 1984. At first glance his testimony appears to lack any scientific basis. Because paroxetine does not exist in nature but, so far as anyone knows, was created for the first time in the early 1970s by Ferrosan, the hemihydrous form could not have existed before then. But it could have come into existence at any time between then and December 1984. It was not *detected* until March 1985, but existence and detection are not the same thing, for we know that HP 23 and HP 24, which are conceded to be hemihydrate, predated the earliest detection of hemihydrate, which was by Curzons in March 1985. The methods available as late as 1985 did not enable detection of small quantities of the hemihydrate in a mixture-smaller than 5 percent at the most. Smaller quantities may have existed ever since the first paroxetine was created.

Bernstein thought not, however, and gave two reasons. First, a batch of anhydrate manufactured by Ferrosan in 1980, though stored in a hot and humid place (the greater the heat—short of the melting point, of course—and the humidity, the likelier is conversion from the anhydrous to the hemihydrous

form), had three years later still not converted to the hemihydrate form, suggesting that it had not been seeded and hence that there were no seeds as late as 1980. And HP 22, manufactured just weeks before HP 23, contained no detectable hemihydrate, whereas HP 23 was entirely hemihydrate. This is evidence that hemihydrate seeds can "metastasize" at a high rate when they come into contact with anhydrate crystals. If so, the fact that HP 23 was the first paroxetine in which the hemihydrate was detected is evidence that there were no seeds before then, that is, before December 1984, and almost certainly not when Ferrosan obtained its patent in 1977. It is true that Curzons in a 1985 memo reported having discovered hemihydrate in a Ferrosan batch dating from 1980, but quite apart from the possibility of later seeding, Curzons convincingly explained that he had been mistaken.

Dr. Terence Threlfall, Apotex's expert on polymorphism, testified to the contrary of Bernstein that anhydrous and hemihydrous forms of paroxetine can coexist happily. There is support for this conjecture in SmithKline's own evidence, of which more later, that some of Apotex's anhydrous product contains small amounts of hemihydrate without conversion of the rest. In other words, as Threlfall testified, a mixture of anhydrate and hemihydrate can be an equilibrium, in which event the earliest batches of paroxetine manufactured by Ferrosan may have contained undetectable quantities of the hemihydrate. In light of this evidence, Dr. Bernstein's absolute certainty that hemihydrate did not exist before December 1984 is not tenable. No one knows when the hemihydrate form of paroxetine came into existence, although it is a reasonable inference that it did not exist in a detectable amount until then.

The conflicting testimony of Bernstein (and also Byrn) on the one hand and of Threlfall on the other can largely be reconciled on the following hypothesis: while the presence of hemihydrate seeds in a batch of anhydrate is likely, provided

the ambient humidity and temperature are no lower than is normal in the temperate zone, to produce conversion within a short time, once the amount converted reaches a few percent of the mixture further conversion is unlikely without substantially greater humidity, temperature, or pressure. In other words, if conversion is plotted against time, then in the case of paroxetine hydrochloride as in the case of the revised process for producing Form I ritonavir, one will observe rapid growth from an initial very low level, followed by a leveling off at a few percentage points. This of course is under *controlled* environmental conditions; given enough humidity, heat, etc., conversion may continue until it reaches 100 percent. By the same token, with much tighter controls less, maybe no, conversion will take place despite the presence of seeds; the clearest case is where there are no water molecules in the environment of the anhydrate.

The Patent and the Patent Controversy

Crystalline paroxetine hydrochloride hemihydrate, along with certain processes for making it (none challenged by Apotex as invalid or contended by SmithKline to be infringed), was patented in patent 723 in 1988, the patent application having been filed in October 1986. After running the FDA gauntlet, the product was placed on the market under the name Paxil in 1993. The patent will expire, as I noted, at the end of 2006. In 1998 Apotex filed an ANDA in which it proposed to manufacture an anhydrous crystalline form of the paroxetine hydrochloride crystal, patent 196 having expired in 1992. Several other generic manufacturers have since filed ANDAs for various anhydrous forms of paroxetine. Apotex was eager to be first because the generic manufacturer whose ANDA is the first to be approved obtains a 180-day period of exclusivity, see 21 U.S.C. § 355(j)(4)(B)(iv)—180 days during which he and the patentee (if as here the patent on the bioequivalent original has not expired) are in effect duopolists. SmithKline deplores

Apotex's eagerness to be first but of course that eagerness is the mirror of SmithKline's zeal to retain the much more extensive protection conferred by a patent that excludes the competition of a bioequivalent drug as infringing.

The reason Apotex waited as long as it did after the expiration of Ferrosan's patent to file its ANDA is that the FDA forbids submission of an ANDA on a "new chemical entity," which crystalline paroxetine hydrochloride hemihydrate is, or its bioequivalent (i.e., the anhydrate), until five years after the patented drug has been put on the market. 21 U.S.C. § 355(c)(3)(D)(ii). The hemihydrate wasn't *really* that new, being bioequivalent to its predecessor, the paroxetine patented by Ferrosan, but it was deemed new because the FDA had never approved the predecessor. See also 21 C.F.R. § 314.108.

As required, the ANDA specified the process of manufacture that Apotex would use to make the product in commercial quantities, and the site, actually sites, of manufacture. The bulk material (the crystalline paroxetine hydrochloride anhydrate before being mixed with excipients and made into pills) would be manufactured in a plant owned by an affiliate of Apotex named Brantford Chemicals, Inc. (BCI). It would then be shipped to a plant owned by another Apotex affiliate, Tor-Pharm, where excipients would be added and mixed, the mixture compressed into pills, and the pills sprayed with an aqueous (88 percent water) coating and bottled for sale. The ANDA represented that Apotex's anhydrous version of crystalline paroxetine hydrochloride would not infringe patent 723. Disagreeing, SmithKline brought this suit, while meanwhile scurrying to obtain patents on other anhydrous polymorphs of the paroxetine hydrochloride crystal; these patents are involved in other litigation between it and Apotex. Since 1998, when Apotex filed its ANDA, SmithKline or its affiliates have applied for almost 100 patents on paroxetine, though not all, or even most, are on anhydrous forms of the molecule.

It may seem odd that SmithKline could obtain *any* patents on anhydrous paroxetine hydrochloride given the expiration of the Ferrosan patent. However, that patent did not refer to paroxetine hydrochloride or to crystallinity, but to a set of compounds of which paroxetine maleate (another paroxetine salt) was one example; and the maleate probably was in amorphous (noncrystalline) form. So there may be room for patents on other salts or other crystals of anhydrous paroxetine. But that is not an issue in this case and I intimate no view on it. Whether manufacturers of brand-name drugs are using follow-on patents to compete unfairly with the generic manufacturers is at present under investigation by the Federal Trade Commission (described in an amicus brief that the FTC filed on January 28, 2003, in *Smithkline Beecham Corp. v. Apotex Corp.*, No. 99-CV-4304 (E.D.Pa.)), but played no role in the trial of this case.

In pretrial discovery SmithKline obtained samples of crystalline paroxetine hydrochloride anhydrate manufactured by Apotex and submitted them for testing to two academic scientists who testified for SmithKline, Dr. David Batchelder and Dr. Thomas Niemczyk. They testified that they had found hemihydrate in the samples and on the basis of this and other evidence SmithKline contends that the manufacture of the anhydrous product by Apotex is likely to infringe patent 723 because some of Apotex's output will consist of hemihydrate. According to SmithKline, the BCI plant is seeded with hemihydrate crystals because it was there that Apotex, exercising the broadened experimental-use privilege conferred by the Hatch-Waxman Act, used and made hemihydrate in the course of developing its anhydrous product. Any seed-bearing bulk material produced by BCI will, moreover, be formed into pills by TorPharm; and SmithKline argues that the compression exerted on the bulk material to make pills, together with the temperature and humidity in the plant and the fact that the final stage of manufacture involves the application of a water-based coating, will promote further

conversion of the anhydrous to the hemihydrous form of paroxetine hydrochloride.

Although crystals of paroxetine can be seen by means of an electron microscope if the crystals are "trapped" on the microscope's stage, there is no technique for detecting minute crystals in particulate matter in a pharmaceutical plant, on a worker's clothing, etc. But it does not follow, as Apotex unguardedly suggests, that the presence of such crystals, the "seed" crystals, cannot be inferred. What is true and important, however, is that the presence of slight amounts of hemihydrate in Apotex's product would not "do anything" for Apotex. The anhydrate has the identical therapeutic properties as the hemihydrate; that is entailed by their bioequivalence, which SmithKline does not contest. And although hemihydrate handles better in the manufacturing process because it is not hygroscopic, this will confer no cost savings on Apotex in the quantities in which it will be present (if at all) in Apotex's product. Dr. Joseph Robinson, an expert on pharmaceutical manufacturing, testified without contradiction that the percentage of hemihydrate in an anhydrate mixture would have to be in the "high double digits" to contribute any commercial value to the mixture. From Apotex's standpoint, any hemihydrate that happens to turn up in its product is a useless byproduct of a manufacturing process that, consistent with the "disappearing polymorphs" theory, is difficult or perhaps even impossible to conduct without producing tiny amounts of the unwanted byproduct. Dr. Bernstein testified that Apotex was indeed trying to manufacture an anhydrous product, while another of SmithKline's expert witnesses, Dr. Batchelder, testified that hemihydrate in an anhydrous product is an "impurity" and SmithKline's lead counsel described anhydrate that contains some hemihydrate as "degraded."

Validity and Claim Construction

There is no infringing an invalid patent. A number of Apotex's challenges to the validity of patent 723 were rejected by Chief Judge Kocoras in pretrial rulings that I am not disposed to reexamine. What is left is, first, a frivolous argument that either patent 196, or an early article that discussed the paroxetine molecule, R. Battegay, M. Hager & U. Rauchfleisch, "Double-Blind Comparative Study of Paroxetine and Amitryptyline in Depressed Patients of a University Psychiatric Outpatient Clinic (Pilot Study)," 13 *Neuropsychobio.* 31 (1985), or both, "literally" (as distinct from "inherently," discussed next) covered the hemihydrate form. There is no mention of hemihydrate in the patent or in the article and the hemihydrate polymorph of paroxetine was unknown either when the patent application was filed or in 1977 when the patent was granted. Nor has Apotex shown that hemihydrate, the invention claimed by patent 723, was obvious given the prior art (patent 196 and the Battegay *et al.* article).

A more plausible argument is that the hemihydrate form was inherent in patent 196 because anyone who followed the directions in that patent would inevitably produce hemihydrate. If it was inherent, it is deemed anticipated, and patent 723 would be invalid. *Atlas Powder Co. v. Ireco, Inc.*, 190 F.3d 1342, 1347 (Fed.Cir.1999); *In re Robertson, supra*, 169 F.3d at 745. Although it was not until seven years after patent 196 was granted that SmithKline chemists at Harlow, and Alan Curzons at Worthing, while following more or less the directions in the patent, produced hemihydrate, the hemihydrous form of paroxetine may have existed earlier and if so the fact that it was not recognized earlier would not defeat a defense of inherency. *MEHL/Biophile Int'l Corp. v. Milgraum*, 192 F.3d 1362, 1365 (Fed.Cir.1999); *Atlas Powder Co. v. Ireco Inc.*, 190 F.3d 1342, 1348 (Fed.Cir.1999); *Abbott Laboratories v. Geneva Pharmaceuticals, Inc.*, 51

U.S.P.Q.2d 1301, 1305-06 (N.D.Ill.1998), aff'd, 182 F.3d 1315 (Fed.Cir.1999). But Apotex has failed to prove this by clear and convincing evidence, as required to invalidate a patent. The serendipitous appearance of a polymorph years after another polymorph of the same crystal is patented does not prove to the requisite degree of certainty that the new polymorph was inherent in the old. In this respect the uncertainties in the scientific community concerning the provenance and causality of polymorphs aid SmithKline because of the heavy burden of proving invalidity coupled with the narrowness with which the Federal Circuit defines inherency. Inherent anticipation "may not be established by probabilities or possibilities. The mere fact that a certain thing *may* result from a given set of circumstances is not sufficient." *MEHL/Biophile Int'l Corp. v. Milgraum, supra*, 192 F.3d at 1365 (emphasis in original); see also *In re Robertson*, 169 F.3d 743, 745 (Fed.Cir.1999); *Glaxo Inc. v. Novopharm Ltd.*, 52 F.3d 1043, 1047-48 (Fed.Cir.1995); *Continental Can Co. USA, Inc. v. Monsanto Co.*, 948 F.2d 1264, 1268-69 (Fed.Cir.1991).

I have been assuming so far that inherent anticipation requires that practicing the old patent invariably produce the new product (the product that is the subject of the challenged patent—here, the hemihydrate—and is contended to have been inherent in the practice of the old patent) *from the moment the old patent was issued.* This may be too strenuous a requirement, though I cannot find any case one way or the other on the point. Maybe it is enough if, because of widespread seeding, by the critical date for anticipation (October 1985, one year before SmithKline applied for patent 723, see 35 U.S.C. § 102(b)) no one who followed the steps outlined in patent 196 for making paroxetine would fail to produce at least some hemihydrate. And this is possible. But again the burden of proof on the issue of validity saves SmithKline. For it is equally possible, as far as anyone knows, that practicing patent 196 in non-seeded premises—and goodness

knows there were some in the United States as of that date—would not have produced any hemihydrate. Cf. *Glaxo, Inc. v. Novopharm Ltd.*, 830 F.Supp. 871, 875-77 (E.D.N.C.1993).

Apotex has still another arrow in its invalidity quiver, however, and that is the argument that the description of claim 1 of patent 723, the only claim in issue, is too indefinite. A patent's specification (the descriptive part of the patent) must "conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention." 35 U.S.C. § 112; see, e.g., *Beachcombers v. WildeWood Creative Products, Inc.*, 31 F.3d 1154, 1158 (Fed.Cir.1994). Claim 1 states simply: "crystalline paroxetine hydrochloride hemihydrate." SmithKline argues that this means what it says, so that even if Apotex's generic paroxetine product contains only a single crystal of the hemihydrate, an undetectable quantity, claim 1 will be infringed. SmithKline correctly notes that the reference group for claim construction is limited to persons knowledgeable about the relevant technology—chemists in this case—and that the four words constituting claim 1 are each of them perfectly clear to chemists and that the four words taken together are also clear to them, at least as a matter of literal interpretation.

Yet until completion of the portion of the trial devoted to the issue of validity SmithKline equivocated between the literal interpretation and a looser interpretation that would add the words "in a detectable amount" to the end of claim 1, or (a reading it preferred) "in a detectable amount whether or not detectable by the methods available when the invention was made or the patent applied for or granted." Eventually, however, though reluctantly, it committed itself to the "single crystal" interpretation, according to which "crystalline paroxetine hydrochloride hemihydrate" includes *all* manifestations of the hemihydrate, no matter how or where produced, or in what quantity relative to the mixture of which

it is a part; even if the production was inadvertent, unavoidable though undesired, and wholly without benefit to the producer or detriment to SmithKline in the sense of cutting into SmithKline's market; and even if the amount is so tiny as to be beyond the limits of detection of any instrument present or foreseeable and the product in which it unexpectedly pops up does not compete with anything made or sold by SmithKline. It need not even be a drug. According to SmithKline, if a worker in a chocolate factory popped a Paxil into his mouth and as a result the factory became seeded with hemihydrate crystals, and the seeds found their way into chocolate that was then sold, the sale would infringe patent 723. (Actually this is wrong; the "first sale" doctrine would allow the worker to do anything he wanted with Paxil tablets that he had bought. The example is saved by assuming that the source of the seeds is a SmithKline executive who picked them up while visiting a seeded SmithKline facility and later visited the chocolate factory.) If the BCI factory is seeded, as it appears to be, all the other drugs that BCI manufactures there, some two dozen or so, may be seeded too and all are thus infringing (if SmithKline's interpretation of claim 1 is correct and does not invalidate the claim) and the company has a slew of additional patent-infringement suits to bring.

This is heady stuff; someone not steeped in patent law might think it loony; and it is not surprising that SmithKline equivocated before embracing the single-crystal theory (embracing it perhaps out of fear that otherwise its proof of infringement would fail—as indeed it would, as we'll see). It continued until the end of the trial to duck and feint by arguing that whether patent 723 claims single crystals is "academic," either because infringement cannot be proved if the infringing component of a mixture is below the limits of detection or because injunctive relief, as in my chocolate example, would be inequitable. The second point is a potentially fatal concession, as I shall point out later. The first is wrong. Being able to detect the presence of hemihydrate

seeds by instruments and being able to infer their presence from circumstantial evidence are not the same. To equate them is a variant of Apotex's erroneous belief that if seeds cannot be "seen" there is no scientific basis for supposing them, or the phenomenon of seeding, to exist.

SmithKline insists that my chocolate hypothetical is "not this case." It is not. But one tests a definition by considering all the things it covers, its "extension" as philosophers say. If someone challenges a definition of "swan" as any bird with a long neck by pointing out that flamingos have long necks, it is no answer that the person offering the definition is not interested in flamingos. It is still an overinclusive definition. SmithKline may not interpret its claim narrowly to avoid invalidity and broadly to prove infringement. *Unique Concepts, Inc. v. Brown*, 939 F.2d 1558, 1562 (Fed.Cir.1991).

Reference to hypotheticals does not violate the principle that "claims may not be construed by reference to the accused device." *NeoMagic Corp. v. Trident Microsystems, Inc.*, 287 F.3d 1062, 1074 (Fed.Cir.2002). As the Federal Circuit had explained in an earlier case, "A claim is construed in the light of the claim language, the other claims, the prior art, the prosecution history, and the specification, not in light of the accused device. . . . [C]laims are not construed 'to cover' or 'not to cover' the accused device. That procedure would make infringement a matter of judicial whim. It is only after the claims have been construed without reference to the accused device that the claims, as so construed, are applied to the accused device to determine infringement." *SRI Int'l v. Matsushita Electric Corp. of America*, 775 F.2d 1107, 1118 (Fed.Cir.1985) (en banc). In other words, the judge is not to say, "I can make everybody more or less happy by first examining the accused infringer's invention and then narrowing the patentee's claim so that it just excludes the defendant's invention, leaving the patent claim otherwise intact." But disallowing that method of claim construction does not

exclude consideration of hypothetical cases as an aid to determining the scope of the claim. My objective is not to protect chocolate makers from being dragged into court by SmithKline (a most improbable prospect, and one which SmithKline expressly disclaimed in its post-trial brief), but to decide whether the claim has limits that render it definite.

The "single crystal" interpretation of claim 1 may be extravagant, but it is not *completely* ridiculous, whatever a layperson might think. The claim is of a product rather than of a method of production; and to make the patentability of a product depend on the percentage of the patented product in a mixture would lead to absurd results. The paroxetine in Paxil is mixed with excipients that constitute 90 percent of the pill by weight, yet no one supposes that the relative weight of the paroxetine in the pill has the slightest significance for patentability. Unlike copyright law, moreover, patent law does not recognize a defense of independent creation. The fact that if Apotex does create hemihydrate as a byproduct of its attempt to manufacture public-domain anhydrate it will not be deliberately "copying" SmithKline is irrelevant.

But there are mixtures and there are mixtures. In a previous order in this case, which SmithKline applauds for holding that hemihydrate does not forfeit patent protection merely by being mixed with something else, Judge Kocoras stated: "It does not necessarily follow, however, as SmithKline would have us believe, that claim 1 covers any modicum of hemihydrate found in any mixture with other substances or polymorphic forms." *SmithKline Beecham Corp. v. Apotex Corp.*, No. 98 C 3952, 2001 U.S. Dist. LEXIS 19766, at *43 (N.D.Ill. Nov. 30, 2001). He went on to say that he thought the claim could be construed in a way that would preserve its validity when read in light of the patent specification, citing *Exxon Research & Engineering Co. v. United States*, 265 F.3d 1371, 1375 (Fed.Cir.2001). He pointed out that some of the properties specified, such as

higher melting point, greater stability, and nonhygroscopicity, "distinguish the new material from prior art anhydrate and thus establish its patentability." *SmithKline Beecham Corp. v. Apotex Corp., supra*, at *45. And he said that he thought there was enough information in the specification to be able to construct a definite meaning for claim 1 and thus save the patent's validity. It falls to me to find that meaning. *Id.* at *47.

Were claim 1 to be interpreted as broadly as SmithKline now contends, it would fail for indefiniteness. (I emphasize that this is not an issue that Judge Kocoras even reached, let alone decided in SmithKline's favor.) The purpose of the statutory requirement of definiteness is to place the members of the relevant technical community on notice of the scope of the patent so that they don't infringe it inadvertently. *General Electric Co. v. Wabash Appliance Corp.*, 304 U.S. 364, 369, 58 S.Ct. 899, 82 L.Ed. 1402 (1938); *McClain v. Ortmayer*, 141 U.S. 419, 424, 12 S.Ct. 76, 35 L.Ed. 800 (1891); *All Dental Prodx, LLC v. Advantage Dental Products, Inc.*, 309 F.3d 774, 779-80 (Fed.Cir.2002); *Solomon v. Kimberly-Clark Corp.*, 216 F.3d 1372, 1378-79 (Fed.Cir. 2000). For remember that inadvertency is not a defense to infringement; there is no defense of independent creation. "The primary purpose of this requirement of definiteness in claims is to provide clear warning to others as to what constitutes infringement of the patent," 3 Donald S. Chisum, *Chisum on Patents* § 8.03, p. 8-18 (2002), because "a zone of uncertainty which enterprise and experimentation may enter only at the risk of infringement claims would discourage invention only a little less than unequivocal foreclosure of the field." *United Carbon Co. v. Binney & Smith Co.*, 317 U.S. 228, 236, 63 S.Ct. 165, 87 L.Ed. 232 (1942), quoted in *Exxon Research & Engineering Co. v. United States, supra*, 265 F.3d at 1375. Stated differently, "if patent infringement can be compared to trespassing, the claims serve as the boundary markers that define what is, or is not, an encroachment on the

inventor's exclusive territory." Alan L. Durham, *Patent Law Essentials: A Concise Guide* 66 (1999).

This purpose cannot always be fulfilled by a literal interpretation. The ordinary meaning of a word can deprive a claim of clarity. *Northern Telecom Ltd. v. Samsung Electronics Co.*, 215 F.3d 1281, 1291 (Fed.Cir.2000). And context can ambiguate as well as disambiguate. Claim 1 must be read against the background of the specification. *Solomon v. Kimberly-Clark Corp., supra*, 216 F.3d at 1378; *In re Moore*, 58 C.C.P.A. 1042, 439 F.2d 1232, 1235 and n. 2 (Cust. & Pat.App.1971). SmithKline acknowledges in its post-trial brief that patent claims are to be interpreted in light of "the patent's specification" as well as the claims language. Patent 723's specification points out the superior handling characteristics of the hemihydrate in the manufacture of a paroxetine salt for therapeutic purposes. This would lead a reader, however technically adept he might be, to suppose that the patented invention was of a crystalline form constituting the active ingredient of a paroxetine-based drug. He would not think the claim extended to the involuntary creation of the crystalline form in quantities so minute as to be of no therapeutic, manufacturing, or other commercial significance and indeed to be undetectable by any means known at the time the patent was applied for and was issued. There is no hint of such a possibility in the patent; the landmine that SmithKline now wants to explode under Apotex is concealed. (Not concealed from Apotex, though, whose CEO expected from the start that SmithKline would sue it.)

An adequate description of claim 1, if indeed the claim embraces even a single crystal created by adventitious seeding, would warn the world of such dangers as are conjured up by the chocolate example. The example may seem fantastic but the reality is alarming enough—as the ritonavir episode recounted by Dr. Bernstein (SmithKline's own witness, remember) illustrates—for any firm contemplating manufac-

ture of a crystalline paroxetine hydrochloride anhydrate, even though it is a public-domain product. "If claim language is vague, competitors must proceed at their peril, and the uncertainty provides the patent owner with what is, in effect, a broader claim." Durham, *supra*, at 68. Not knowing how far claim 1 reaches, competitors might steer clear of producing a product that would infringe the patent under the patent's broadest possible interpretation. And not just competitors, as we know from the chocolate example. There would be the kind of "chilling" effect of which the courts speak when they are considering First Amendment challenges to vague or overbroad regulations of speech.

Suppose that Apotex, reasonably assuming that no one could claim with a straight face that a single crystal inadvertently created as a result of accidental seeding would make Apotex an infringer of claim 1 of patent 723 and thus prevent the FDA from granting its ANDA, spent a billion dollars on making sure that BCI would produce no more than 100 molecules of hemihydrate in any batch of its anhydrate product. Would it be unreasonable in interpreting claim 1 as not claiming for SmithKline the exclusive right to those molecules? I think not. I am not even sure that SmithKline would disagree. Instead it probably would say that that is not our case either, because Apotex did not make *heroic* efforts to avoid producing even undetectable amounts of hemihydrate, as in my example. This point may bear on infringement but it does not bear on claim construction; to repeat, a patent claim is not definite if it does not make the claim's limits clear. I take SmithKline's equivocations to be tacit acknowledgements that those limits are not clear.

I am inclined, however, rather than to declare claim 1 invalid for indefiniteness to interpret it as excluding hemihydrate produced by involuntary conversion of a proportion of an anhydrous mixture so small as to lack any commercial significance. The Federal Circuit favors giving a claim a

narrowing construction to avoid invalidating it for indefiniteness, *Exxon Research & Engineering Co. v. United States, supra*, 265 F.3d at 1375-77; *ACS Hospital Systems, Inc. v. Montefiore Hospital*, 732 F.2d 1572, 1577 (Fed.Cir.1984), even if the patent claim "poses a difficult issue of claim construction." *Exxon Research & Engineering Co. v. United States, supra*, 265 F.3d at 1375. My construction produces a claim with definite, readily observable boundaries because Apotex's manufacturing methods, and those of other producers of anhydrous forms of paroxetine, will produce hemihydrate, if any, in quantities far below the "high double digits" level at which hemihydrate in a mixture with anhydrate attains commercial significance. There is no risk of inadvertent infringement and hence of giving the patent an *in terrorem* effect beyond its valid scope, if my construction is correct.

In adopting the "any commercial significance" construction I am not converting a product claim to a process claim, because the patented invention remains the product whatever the process used to make it. Nor am I suggesting that the presence of trace elements of a patented product can never be infringement, for reasons illustrated by the facts of *Northern Telecom Ltd. v. Samsung Electronics Co., supra*, on which SmithKline relies without acknowledging the wholly different situation described in that case. Nor am I taking undue liberties with the claim's "plain meaning." Literal interpretations that produce absurd results are regularly rejected in contractual and statutory interpretation, *Public Citizen v. U.S. Dept. of Justice*, 491 U.S. 440, 453-55, 109 S.Ct. 2558, 105 L.Ed.2d 377 (1989); *Level 3 Communications, Inc. v. Federal Ins. Co.*, 168 F.3d 956, 958 (7th Cir.1999); *Marlowe v. Bottarelli*, 938 F.2d 807, 812 (7th Cir.1991); *Outlet Embroidery Co. v. Derwent Mills*, 254 N.Y. 179, 172 N.E. 462, 463 (1930) (Cardozo, J.), and the Federal Circuit deems statutory interpretation a useful analogy to claim construction. *Markman v. Westview Instruments, Inc.*, 52 F.3d 967, 987 (Fed.Cir.1995),

aff'd, 517 U.S. 370, 116 S.Ct. 1384, 134 L.Ed.2d 577 (1996). The single-crystal interpretation of claim 1 has absurd consequences that do not serve any policy of patent law. "General descriptive terms will *ordinarily* be given their full meaning." *Johnson Worldwide Associates, Inc. v. Zebco Corp.*, 175 F.3d 985, 989 (Fed.Cir.1999) (emphasis added). This is the rare case in which the qualification that I have italicized comes into its own, and for the reason stated in the case just cited: where the ordinary meaning of a term deprives a claim of clarity, rendering it indefinite. *Id.* at 990.

My approach to the interpretation of claim 1 is supported by the oldish but still goodish case of *Corning Glass Works v. Anchor Hocking Glass Corp.*, 374 F.2d 473, 475-79 (3d Cir.1967). The patent covered crystallized glass (Corning Ware, which looks like porcelain) and described the product as being "at least" 50 percent crystalline. Apparently there was no way to measure the percentage of crystallinity precisely, and on that basis the district court held the patent unenforceable because he thought it would be too difficult for a competitor to determine whether its product was "at least" 50 percent crystalline. The court of appeals reversed. The court looked to the purpose of the invention, which was to create a "material with substantially different properties [from conventional glass], predominantly crystalline." There had been testimony that the percentage was not really the point; the point was the changed properties of the material compared to noncrystalline glass. And these were apparent on inspection. The court forwent literalism to uphold rather than defeat the patent's validity, and that is what I am doing here.

Even closer to the present case, in light of SmithKline's insistence that claim construction must never add words to the words of the claim, is *Multiform Desiccants, Inc. v. Medzam, Ltd.*, 133 F.3d 1473, 1477-78 (Fed.Cir.1998). There, on the basis of the patent specification, the Federal Circuit held that "degradable" meant "degradable only by dissolu-

tion," though the additional words did not appear in the claim itself, but were added by construction. See also *Laitram Corp. v. Morehouse Industries, Inc.*, 143 F.3d 1456, 1463 (Fed.Cir.1998); *C.R. Bard, Inc. v. M3 Systems, Inc.*, 157 F.3d 1340, 1350 (Fed.Cir.1998).

Infringement

If the interpretation of claim 1 of patent 723 that I have adopted (crystalline paroxetine hydrochloride hemihydrate in any quantity sufficient to have any commercial significance) is sound, and claim 1 therefore valid, then it is clear that there is no infringement and the case is over. This makes SmithKline's victory on validity somewhat Pyrrhic, but only somewhat, since if the patent were invalid the generic manufacturers could make the hemihydrate form, whereas if they are confined to anhydrous paroxetine they have to reckon with SmithKline's imposing array of recently acquired anhydrate patents.

Noninfringement is easily shown under the narrow interpretation of claim 1 because SmithKline has failed to prove that even when Apotex increases production of its generic anhydrate to full commercial scale, if it is ever permitted to do so, the proportion of hemihydrate in the product is likely to exceed one or two percentage points, a level far too low to produce any benefits whatsoever to Apotex. (It hasn't even proved that the proportion of hemihydrate in Apotex's product will reach those levels, but that is for later.) But since the Federal Circuit may disagree with my interpretation and may also disagree that a broader interpretation would render claim 1 invalid for want of a definite description, prudence, coupled with the fact that the issue of infringement was fully tried, impels me to push on and, assuming that the patent is valid even when read broadly, decide whether patent 723 is likely to be infringed by the methods that Apotex intends to use to manufacture its anhydrous product. The

burden of proof to show infringement is of course on SmithKline.

Whether SmithKline has proved infringement under the broadest, the "single crystal," interpretation of claim 1 could in principle (though not in practice) depend on the answer to the following esoteric legal question: if a single hemihydrate seed escaped from a Paxil tablet that was on BCI's premises in the mid-1990s, and it has been floating about BCI's plant ever since and it will find its way into a batch of anhydrous material that the plant produces and eventually into a pill that is sold to the public, would Apotex, though not guilty of infringing SmithKline's exclusive right to *make* the patented product, be guilty of infringing either of the other rights that a patent confers, namely the right to use or the right to sell (or offer to sell) the patented product? 35 U.S.C. § 271(a). Maybe not. Quite apart from the first-sale doctrine that I mentioned in discussing the first version of the chocolate-factory hypothetical, Apotex would not be *using* the seed in any intelligible sense of the word, since hemihydrate in small amounts does nothing for the anhydrate with which it is mixed. And it would not be *selling* it in a meaningful sense either, since the presence of a single seed would not increase the value to consumers and hence the price that Apotex could charge for the anhydrate, or reduce Apotex's costs of production or sale, by even a Canadian penny.

I need not try to wrestle this question to the ground (though I note that if the answer is "no," it at least nixes the argument that the chocolate manufacturer in the second version of the hypothetical, the one to which the first-sale doctrine did not apply, would be infringing, for seeds of paroxetine hydrochloride hemihydrate will not convert chocolate to paroxetine hydrochloride hemihydrate). Its factual premise is unrealistic. If BCI produces bulk material that contains hemihydrate seeds, even in a very small number, some undoubtedly will be crystals that BCI made, rather than all being

leftovers from mid-1990s experimental uses. It is true that BCI is trying to minimize the amount of hemihydrate that its production process creates—SmithKline's argument that Apotex is indifferent to the amount of hemihydrate its production process creates is unsound, because the more hemihydrate there is the more vulnerable Apotex is to charges of patent infringement. But because BCI's plant is seeded as a result of the mid-1990s experiments, and because the anhydrate as it proceeds through the process will at several junctures be exposed to air that contains enough water molecules to permit conversion of anhydrate to hemihydrate, BCI probably will be "making" at least some hemihydrate crystals and therefore infringing, at least prima facie, patent 723 if claim 1 is interpreted to cover single crystals of the hemihydrate. And although a handful of crystals in a batch of the anhydrate is not detectable in the sense that its presence can be determined by a test, I pointed out earlier that the presence of a substance may be inferable even when it cannot be detected by instruments however sensitive. That is the situation here. *Some* conversion from anhydrate to hemihydrate is likely to occur in a seeded facility in which the anhydrate is exposed to air; BCI's plant is seeded; and the anhydrate manufactured there is exposed to nondehumidified air before it leaves the plant. This evidence is sufficient to support an inference that BCI will be making at least tiny amounts of the hemihydrate if it is permitted to manufacture the anhydrate. But I have rejected the "single crystal" interpretation of claim 1 of patent 723.

An intermediate interpretation between "single crystal" and "any commercial significance" deserves consideration, however. It is one that SmithKline has flirted with and will doubtless embrace as a fallback if my rejection of the single-crystal claim construction stands. The fallback interprets "crystalline paroxetine hydrochloride hemihydrate" as being limited to detectable amounts of the compound.

Such an interpretation makes the issue of infringement more complicated and uncertain than either of the other two interpretations that I have been examining. I must consider to begin with whether "detectable" means detectable when the patent was applied for back in 1986 (or in 1988, when the patent was granted, but nothing turns on the choice between these dates, though the only case I can find supports the earlier one, *Raybestos-Manhattan, Inc. v. Texon, Inc.*, 268 F.2d 839, 842 (1st Cir.1959)), rather than today, when as a result of better methods the limits of detection are lower. It is true as Judge Kocoras ruled that to prove infringement a patentee is not limited to the means of detection that existed when the patent was issued, any more than the prosecution in a criminal case is forbidden to use a means of detection (say, a DNA test) that did not exist when the statute creating the offense was enacted or when the crime was prosecuted. But the question is not whether SmithKline can use new methods of detecting the presence of polymorphs to prove that Apotex's anhydrate will contain hemihydrate. It is whether "detectable quantities" should be limited to quantities of hemihydrate that were detectable by the technology of the time. Someone who wanted to manufacture a product that did not infringe claim 1 could not make an informed decision on whether or how to proceed with his project were he at risk that unforeseen technological advances would result in his being declared an infringer. His uncertainty would deter innovation and thus offend patent policy. The "detectable back then" approach has the advantage that "it does not cause the patent to mean one thing at the time of its issuance and another at some later date upon the discovery of a more accurate test." *Id.* at 842.

Apotex is not an infringer under this interpretation of claim 1. When SmithKline obtained patent 723 the limit of detection of the hemihydrate when mixed with an anhydrate was between 5 and 8 percent. Apotex is unlikely to produce an anhydrate that contains such a high percentage of

hemihydrate. True, if there are enough seeds, a sufficiently humid atmosphere, sufficient heat, strong pressure, and plenty of time, conversion to a higher percentage is likely. In an early experiment conducted by SmithKline, samples of anhydrate taken from HP 12—a batch that had been made before 1982, which in all likelihood was before the hemihydrate came into existence—were seeded with 2 percent and 4 percent hemihydrate. After the seeded samples were exposed for a week to a temperature of 37% A1 Centigrade (99° Fahrenheit) and a relative humidity of 75 percent, conversion was observed—complete conversion with the 4 percent seeding and conversion to "largely" hemihydrate with the 2 percent seeding. P.C. Buxton, I.R. Lynch & J.M. Roe, "Solid-State Forms of Paroxetine Hydrochloride," 42 *Int'l J. Pharmaceutics* 135 (1988).

BCI studies of several batches made by it in 1997 showed small amounts of conversion to hemihydrate after nine months. These batches had been produced in a pilot operation, however, and Apotex presented persuasive evidence at trial that BCI's current manufacturing methods are less likely to cause conversion. SmithKline contends that experiments that Dr. Keshava Murthy, a chemist who is currently BCI's president, conducted on batches made in 2000 revealed conversion, but I reject the contention below. SmithKline also points to a sample from one batch made by BCI in 2001 that it claims contains 75 percent hemihydrate. This is a real outlier, however—and an unconvincing one. The estimate comes from Dr. Niemczyk's eyeballing of the spectrum of the sample. When he was asked how one can determine the percentage of a particular substance in a mixture by merely a visual inspection of the mixture's spectrum, his answer was perfunctory and unconvincing. I conclude that no recent batches produced by Apotex have been reliably shown to contain hemihydrate at the limit of detection (5 percent) of the standard tests.

Remember that I have to make a *predictive* judgment: the issue is not, has BCI produced any hemihydrate, which unquestionably it has, if only when it was exercising its Hatch-Waxman rights, but will it do so (and here I am considering whether it will do so in a quantity equal to at least 5 percent of the anhydrate mixture) if and when it is permitted to go into full production. Apotex presented evidence that its current system of production, which incorporates a variety of measures designed to minimize conversion, such as minimizing the exposure of the anhydrate to air or other sources of water, will enable it to hold the percentage of the hemihydrate in its anhydrate product far below 5 percent. The ambient temperature will be much lower than 99° F, the relative humidity much lower than 75 percent, most of the production process will be conducted in vacuum-sealed reactors so that the aggregate period of exposure to the air will fall far short of 168 hours, and the quantity of seeds deposited in the paroxetine during the production process will be much less than 2 or 4 percent. Those figures are closer to the maximum plausible estimate of the level of hemihydrate *after* conversion by adventitious seeding notwithstanding a controlled environment.

SmithKline argues that scaling up from pilot production to full commercial production is bound to increase the likelihood and extent of conversion. Dr. Bernstein acknowledges, however, that little is known about the effects of scale-up on conversion. Bernstein, *supra*, at 256. And because Apotex has a powerful incentive to minimize the amount of hemihydrate in its commercial production in order to avoid future suits for infringement, there may well be *less* hemihydrate in the scaled-up than in the pilot phase of production. And here uncertainty operates against SmithKline because the burden of proof on infringement rests on it rather than on Apotex. The burden is not carried by the recitation of generalities about humidity, pressure, heat, and seeds being the risk factors for conversion; they are the risk factors, but

what is missing is a formula that would relate them, at the level they are likely to attain in BCI's mature production process, to the probability and amount of conversion.

SmithKline further argues, however, that even if the bulk anhydrate that BCI produces and ships to TorPharm for tableting will contain only seeds of the hemihydrate, the heat and humidity in the TorPharm plant, and particularly the pressure exerted on the bulk material to form it into tablets, will, if there are seeds in the bulk material, surely cause conversion to the hemihydrate in a higher percentage than 5 or 8. Beware "surely"; the evidence, presented by SmithKline's experts Byrn and Dr. Christopher Rhodes, is unconvincing. As in the case of BCI's production of the bulk material, with the burden of proving infringement on SmithKline the scientific uncertainties concerning polymorphism in general and the paroxetine polymorph in particular work against SmithKline rather than against Apotex. All Rhodes could say was that there would be heat, pressure, etc. in TorPharm's production process; he could not say how much. All Byrn could say was that the hotter the plant, the greater the pressure, etc., the more likely was conversion, but he could not say how much more likely or what percentage of the paroxetine in the final tablets would be hemihydrate. We know that moisture is a necessary condition for conversion of the anhydrate and also that at pressures much higher than anything likely to be encountered in Apotex's tableting process the combination of seeds, adequate moisture, and pressure constitutes a set of sufficient conditions for conversion to occur. Even in that case, however, we do not know how much conversion will occur. And no evidence was presented that would permit an inference, when the pressure does not reach the critical level, that Apotex is more likely than not to produce an anhydrate mixture that contains more than 5 percent hemihydrate.

SmithKline did not seek to conduct tests in BCI's or TorPharm's plant to determine whether the manufacture of the bulk or finished anhydrate would create hemihydrate. It could have gotten a court order allowing it to do so, had Apotex balked. And in jousting with BCI's Dr. Murthy over the latter's testimony that a finding of hemihydrate in a test of the anhydrate was a false positive, SmithKline's lawyer acknowledged that adventitious seeding is a hit-and-miss phenomenon. The test in question had been repeated because the positive result was unexpected (not to mention undesired!). The retest revealed no hemihydrate and this led Murthy to conclude that the first result had yielded a false positive. The lawyer countered by remarking that the first test might still be evidence of seeding, because seeding might have affected only the first test: "Sir, isn't it quite possible that the seed was in the laboratory on that day when you measured it, but the seed wasn't on the testing pan the next time you measured it?" This insinuation undermines SmithKline's theory that once there are seeds in a facility, conversion to detectable levels of hemihydrate is highly likely even if precautions are taken, such as minimizing exposure to air, controlling temperature, humidity, and the force of compression, and adding desiccants.

Murthy also testified about the results of repeated tests on another batch. The first test had been conducted three months after the batch was created and was positive for hemihydrate. The test was immediately redone and was negative. The test was repeated at six months with a negative result, 12 months (positive), and 18 and 24 months (both negative). Murthy thought the two positive test results must have been false positives because if a batch reveals conversion at time *t* more conversion can be expected at any subsequent time; almost all the tests in evidence in this case showed more conversion the greater the lapse of time since the anhydrate being tested was produced and none showed conversion declining with time. The lawyer challenged Murthy by suggesting that the tests

might have been on samples from different locations in the barrel of anhydrate. Maybe so, but this implies that the hemihydrate and the anhydrate can coexist in an equilibrium.

I also find it significant in predicting how much hemihydrate is likely to be found in Apotex's product that SmithKline did not commission or conduct any controlled experiments on seeding. It could have found a facility in which hemihydrate seeds were unlikely to be present, made anhydrate there, let the anhydrate sit around long enough to indicate that it wasn't going to convert (this would be evidence that the facility was indeed unseeded), then made the hemihydrate and then the anhydrate again and seen whether and when and under what environmental conditions of heat, pressure, humidity, and impurities and to what extent (5 percent? 50 percent? 100 percent?) it converted to hemihydrate. SmithKline also failed to test all the samples of Apotex's product, both bulk material and pills, that Apotex produced in response to SmithKline's discovery requests, and I never got a satisfactory answer as to how the selection was made. SmithKline also failed to conduct more than one type of test on any sample (with an irrelevant exception involving some DSC tests that Dr. Byrn conducted with inconclusive results), although multiple testing is *de rigueur* when seeking to identify a substance that is only a small part of a mixture that contains closely related substances (such as different polymorphs of the same, or nearly the same, molecule). And it did not follow through on Dr. Bernstein's suggestion as to how one might try to re-create a less stable polymorphic form after a new, more stable form had appeared. Bernstein, *supra*, at 93. Of course Apotex could have done more testing too, but in a finger-pointing contest SmithKline must lose because it bears the burden of proving infringement.

At trial SmithKline repeatedly found itself coming and going on the question whether Apotex's product is likely to contain at least 5 percent hemihydrate. To refute Apotex's

claim that if its product contains *that* much hemihydrate Ferrosan's must have contained *some* and so hemihydrate was invented and indeed patented in patent 196 and therefore could not be patented later, SmithKline effectively refuted the inconclusive spectroscopic evidence (which focused on the "Jacewicz shoulder" and the "Niemczyk tail," ambiguous indications of the presence of hemihydrate in infrared spectra) that Apotex presented with regard to hemihydrate in Ferrosan's anhydrous product. The same inconclusiveness, however, dogged SmithKline's effort to establish by conventional methods (that is, the methods that have a 5 to 8 percent limit of detection, such as visual inspection of infrared spectra, x-ray powder diffraction studies, and differential scanning calorimetry) that either bulk material or pills produced by Apotex contain that much hemihydrate.

In sum, I am not persuaded that Apotex will produce an anhydrate that has sufficient hemihydrate to be detectable by the methods in use in 1985. But now suppose that "detectable amounts" in the "detectable amounts" interpretation of claim 1 means detectable by any method, however recent. (So here is a fourth possible construction of claim 1 that I am considering.) This interpretation would raise a serious question of indefiniteness, though one I shall not try to answer. As science develops finer and finer instruments for the detection of polymorphs, the "detectable by any means" and "single crystal" interpretations approach convergence. A claim construction that places a potential infringer at the mercy of scientific advances that may be unpredictable suffers from the same infirmities as the single-crystal interpretation and therefore might if adopted invalidate the patent. But I shall limit my consideration to the question whether SmithKline has proved infringement under this interpretation of claim 1.

Two of SmithKline's expert witnesses, Drs. Niemczyk and Batchelder, claimed to have detected hemihydrate in samples of Apotex's anhydrate product in amounts below the old 5-8

percent limit of detection. Niemczyk used a statistical technique called "partial least squares" that is designed to extract more information from a spectrum than any of the older methods. Apotex tried to convince me that it is an unproven method and was misapplied by Niemczyk. I reject the first point. Partial least squares has in recent years become a standard method for detecting the presence of a specific crystalline form. See *Glaxo Group Ltd. v. TorPharm, Inc.*, 153 F.3d 1366, 1373 (Fed.Cir.1998). Dr. Niemczyk is an experienced practitioner of it but I do not credit his testimony that he was able to detect small amounts (down to a tenth of one percent) of hemihydrate in five of the nine samples of Apotex's anhydrate that he tested.

The first step in using PLS to determine the composition of an unknown mixture is to create a reference sample (or samples) comprising a mixture of known proportions of known substances. The spectrum of that mixture (an infrared spectrum in this case, though PLS can be applied to other spectrographic methods as well) is then compared with the spectrum of the mixture whose composition is sought to be determined. A visual comparison of spectra will not detect an amount of hemihydrate smaller than 5 percent of a mixture with anhydrate. This is where PLS comes in.

The key concepts in PLS analysis are "factors," "degrees of freedom" (each degree of freedom corresponds to one causal or explanatory variable), and "spectral F ratios" (a measure of statistical significance). Each substance in a mixture will generate its own spectrum, making the spectrum of the mixture a composite. With the aid of a computer, the PLS analyst "factors" the composite spectrum into its components, much as one would factor a number. Niemczyk required 14 factors to decompose his reference spectra. He next had to select the number of independent variables needed to explain the composite spectrum and thus identify the constituents of the mixture that had generated the spectrum. He picked the

number four, because he believed that only four things would influence the spectrum. These were the amounts of anhydrate and hemihydrate in the mixture, the amount of Nujol mull (a gel applied to the mixture to enable spectroscopic measurement) in it, and the mixture's thickness.

To determine whether a batch of anhydrate produced by Apotex contained 1 percent hemihydrate, Niemczyk created a reference sample consisting of anhydrate and hemihydrate in a ratio of 99 to 1, plus the Nujol mull; obtained the infrared spectrum of that sample; and then compared it (not by visual inspection but by means of the PLS formula) with the spectrum of the test sample. If the spectra were identical, the comparison would show that the test sample contained 1 percent hemihydrate. He created other reference samples to test for other possible percentages of hemihydrate in the Apotex samples as well. He estimated intermediate percentages by extrapolation.

One of Apotex's expert witnesses, Dr. Peter Griffiths, contended that the number of degrees of freedom must equal the number of factors (minus one, but that is a technical detail that I can ignore). Niemczyk's analysis contained only four degrees of freedom, corresponding to the four independent variables that he identified, even though he used 14 factors. The significance of this point is that the more degrees of freedom employed in a PLS test, the more exacting are the criteria of statistical significance. To attain significance at a given level (such as 95 percent), the spectral F ratio must not exceed a specified level, and that level is lower the greater the number of degrees of freedom. Had Niemczyk used 14 degrees of freedom, the spectral F ratios that he obtained in his PLS tests of hemihydrate in Apotex's product would have been too high to be statistically significant.

Griffiths' criticism would be compelling if every factor (that is, every component of the reference spectrum) had to have a separate cause; then the need for 14 factors to

decompose the spectrum would show that Niemczyk had failed to identify all the independent variables in play. As Niemczyk explained, however, if the spectral effect of a variable is nonlinear, several factors may be required to account for the nonlinearities, but the additional factors would not correspond to additional variables and so there would be no need to jack up the number of degrees of freedom and correspondingly lower the significance ceiling on the spectral F ratio.

Griffiths also questioned Niemczyk's method of determining the standard deviations of his estimates of the amount of hemihydrate contained in the Apotex samples that he examined. Suppose that the mean estimate of the percentage of hemihydrate in a sample were 5 percent with a standard deviation of 1 percent. Then the probability that the true value was between 3 percent and 7 percent, that is, within two standard deviations of the mean estimate, would be 95 percent, a standard measure of statistical significance. But if instead the standard deviation were 3 percent, the 95 percent confidence interval would run from -1 percent to +11 percent, and one would not be 95 percent sure that the sample in question actually contained a positive (>0%) amount of hemihydrate.

Dr. Griffiths was correct—the standard deviations computed by Dr. Niemczyk were too small, as Niemczyk essentially conceded when recalled to the stand after Griffiths testified—and as SmithKline essentially concedes, as well, in its post-trial brief. For there, instead of trying to defend Niemczyk's method, SmithKline states merely that, using Griffiths' method of computing the standard deviation, "Professor Niemczyk can still conclude with at least 80% to 85% confidence that five of nine of Defendants' batches contain measurable amounts of hemihydrate." This need not be a fatal concession, since 95 percent (i.e., a 5 percent probability that the sign of the coefficient being tested would

be observed in the test even if the true value of the sign was zero) is an arbitrary measure of statistical significance. This is especially so when the burden of persuasion on an issue is the undemanding "preponderance" standard, which requires a confidence of only a mite over 50 percent. So recomputing Niemczyk's estimates as significant only at the 80 or 85 percent level need not be thought to invalidate his findings. But he did not recompute them, and so there is no evidence that his findings are significant at or even near those levels.

There are more problems with Niemczyk's evidence. SmithKline's lawyers gave him an anhydrate that SmithKline had created and dubbed "Form A"—had in fact patented (remember that SmithKline has patented various anhydrate crystals of paroxetine)—as well as the hemihydrate contained in Paxil, to be his reference samples. After Niemczyk created the reference samples and determined their spectra, the lawyers gave him batches of the bulk material that BCI ships to Tor-Pharm for tableting. As we know, however, there are several anhydrate polymorphs of paroxetine besides Form A. There is of course Form 2, the anhydrate crystal before the hemihydrate appeared. There are also Forms B, C, and D. All five of these polymorphs are manufactured by SmithKline. There is also a sixth polymorph of paroxetine, a solvate containing molecules of isopropyl alcohol (the solvent). There is also Form Z, which is what Apotex calls the anhydrate that it is manufacturing. Form Z appears to be either the same as, or very similar to, Form 2, which is what SmithKline was manufacturing before it switched to the hemihydrate. Of all the anhydrous forms of crystalline paroxetine hydrochloride, Form 2 is the one most likely to be within the public domain, so it is logical that Apotex's Form Z would track it closely.

All crystalline forms of paroxetine yield similar though not identical spectra, since all contain paroxetine molecules as their predominant component. That makes it important in a

test for the presence of hemihydrate to be certain that the reference sample of anhydrate is of the same form as the anhydrate in the mixture to be tested, that is, in the Apotex samples. What is more, Apotex's samples contain impurities, each with its own spectrum signature. They are not the same impurities as in the reference samples, and spectra of different substances can be confusingly similar. An impurity in an Apotex sample could conceivably cause the sample's spectrum to be mistaken for the spectrum of a mixture containing hemihydrate.

What Niemczyk was doing, under the direction of the lawyers who had hired him, was comparing the spectrum of a mixture consisting of a 99:1 ratio of Form A anhydrate to hemihydrate (I need not discuss his other reference samples separately, which involve different ratios of Form A to hemihydrate), plus no doubt some impurities, with the spectrum of a mixture containing Apotex's Form Z (≈ Form 2) anhydrate, other impurities, and—maybe—a small amount of hemihydrate. Maybe. An alternative possibility, however, is that the spectrum of Apotex's Form Z anhydrate mixture, when compared with the spectrum of the quite different mixture that Dr. Niemczyk was told was to be his reference sample (the Form A mixture supplied him by the lawyers), revealed differences that were mistaken for proof that there was hemihydrate in the Apotex mixture.

Niemczyk had received another mixture from SmithKline, this one containing Form Z anhydrate manufactured by SmithKline. He had intended to determine its spectrum for possible use as a reference spectrum. It would have been the natural choice for a reference sample for a test of Apotex's mixture, which was also Form Z. But the lawyers told him not to test it, and he did not. Nor did they give him all the samples they had obtained of Apotex's product. Nor did they give him a variety of samples to test without telling him

which were Apotex's. He knew what they wanted him to find, and he found it.

Was there *really* hemihydrate in Apotex's product in an amount detectable by the PLS method, or was Niemczyk's finding an artifact of the methodology that the lawyers imposed on him? My confidence in his testimony was shaken by the fact that his procedure had been manipulated by the lawyers—for reasons, by the way, that were never explained either to him or to me. I am particularly disturbed by their having forbidden him to test the Form Z sample as part of the process of creating reference samples. It was the one closest to Apotex's product and therefore the prime candidate to be the reference sample for a test of that product. I am also distressed by his failure to insist that they send him a variety of mixtures to test of which only one or a few would be Apotex mixtures. Moreover, as with any test, one wants the tester to be "blind." Dr. Niemczyk did not conduct a blind-fold test of the Apotex samples.

I do not gainsay Niemczyk's claim, supported by most of the other witnesses, that every crystal generates a unique spectrum, just as every human being has, or so it is believed, a unique set of fingerprints. The question is the power of his methodology to discriminate among the different spectra generated by similar crystals. If you compared the sharp photograph of one person's fingerprints with a blurred photo of another person's fingerprints, you might conclude that they were the same person. The same kind of thing may well have happened here.

Dr. Batchelder is an expert in Raman microscopy, another recent but accepted method of determining the presence of small quantities of a given substance in a mixture. (Raman spectroscopy, as distinct from microscopy, is much older.) The Raman microscope plays a fine laser beam, only two microns in diameter (a micron is one one-thousandth of a millimeter), across the mixture, in effect sampling the parti-

cles that constitute the mixture. When the beam hits a particle, the particle scatters the beam in much the same way that a prism refracts light, producing (like the prism) a spectrum similar to that produced by infrared spectroscopy. Batchelder had to construct reference spectra and like Niemczyk he based these on an incomplete array of anhydrate forms (A, B, and C, but not D or Z, or the excipients used by Apotex—unlike Niemczyk, Batchelder was given pills to test, not the bulk material) furnished him by SmithKline's lawyers. With these spectra in hand he scanned samples of Apotex's anhydrate provided to him by SmithKline, hitting occasionally, according to Batchelder, crystals that generated the characteristic Raman spectrum of paroxetine hydrochloride hemihydrate. He got a higher reading when the laser was focused on the edge of the Apotex tablets, and he surmised that this was because in the last step of their production the tablets are sprayed with an aqueous coating. (His surmise was not admissible evidence, as he is not an expert in the manufacture of pharmaceuticals.) Although the average percentage of hemihydrate "hits" in the edge scans exceeded 8 percent, he explained that this figure could not be translated into an average weight of hemihydrate in Apotex's tablets. The edges are believed to contain more hemihydrate than the core of the tablets; more important, a percentage of Raman hits cannot be translated into a percentage of weight.

Apotex to the contrary notwithstanding, Raman microscopy is, potentially at least, a reliable method of determining the presence of hemihydrate in a mixture. The problem again lies with the lawyers' "feeding" of the expert. They gave Dr. Batchelder Apotex samples that were old and might have converted to hemihydrate under conditions not duplicated in BCI's and TorPharm's current production system. Further feeding occurred when, because Dr. Batchelder had no experience in doing Raman microscopy on drugs, the leader of SmithKline's team of Raman microscopists, Dr. David Lee, instructed him in the preparation of a sample for a Raman

scan—how and with what to slice the tablet, which tablets to scan, and what location on the tablets to scan.

Batchelder was aware of though not highly sensitive to the danger of conversion, and to reduce it he substituted epoxy resin for hot wax in preparing each sample for the microscope—but the pills were left in the open air while the epoxy was drying. And he performed his Raman tests on Apotex's pills in a SmithKline facility that is seeded with hemihydrate. SmithKline, which throughout the trial was constantly rounding on Apotex for failing to take this or that precaution to prevent anhydrate from being exposed to air during the manufacturing process, was remarkably indifferent to that danger when its experts were conducting the tests that it hoped would reveal the presence of hemihydrate. It's as if SmithKline's lawyers had asked Apotex's witnesses: "Why didn't you do what we didn't do?"

One of Dr. Batchelder's assistants, a Dr. Webster, in slicing Apotex's pills to prepare their contents for the microscope, used a nondisposable brush to wipe the blade after each slice. The brush was kept clean by "dusting," and so may have been infested with hemihydrate seeds that the brush transferred to the blade and thence to the mixture to be examined under the microscope. In addition, Webster's lab book states that he regularly brushed debris off the *pills* as well as off the blade. Batchelder testified that he didn't think Webster had actually brushed the pills; "I just think this is slightly sloppy writing within his lab book." I would be more impressed if Webster, the author, had testified about the entry in his lab book. He did not. And Batchelder did not comment on Webster's testimony that he had brushed the blade.

Dr. Lee and his team are highly experienced in conducting Raman tests of drug samples, including tests to determine the presence of paroxetine hydrochloride hemihydrate in a mixture. Yet SmithKline never asked Lee or his team to test

Apotex's samples for hemihydrate. (SmithKline refers for the first time in its post-trial brief, without citation, to a protective order that it claims forbade Lee to analyze Apotex's samples. When at the trial I asked Lee why he hadn't been the one to perform the tests, he said the lawyers had told him they needed an outside expert; that would have been lawyers' cue to mention the protective order, but they did not.) Instead he was directed to teach Batchelder how to do it. He told Batchelder to keep careful notes of the instruction and after completing it gave him a test to make sure he'd learned how to use Raman microscopy to determine the presence of paroxetine hydrochloride hemihydrate in an anhydrate mixture. In other words, the *real* expert was an employee of the defendant, and the nominal expert was a novice in testing mixtures for hemihydrate who had to be taught by the employee.

Whether because of inexperience or incomplete instructions, Batchelder omitted precautions that would have enhanced the reliability of his results. I have mentioned some of these omissions and here I add that given the possibility that the laser beam itself might cause conversion, he should probably have examined the same anhydrate crystal at intervals to see whether the crystal had altered its composition in the interim. There was an inconclusive back and forth at trial about whether the beam (which is not hot) could precipitate conversion; the issue could have been resolved long before trial, by proper experimentation by Dr. Batchelder—or Dr. Lee, the real expert on Raman microscopy of drug polymorphs.

Although Lee is an employee doubtless loyal to SmithKline, expert witnesses are not known for biting the hand that feeds them, he was very generously. Dr. Batchelder has been paid almost $[illegible],000 for his work in this case. (SmithKline has paid its testifying experts in this case almost $1 million; Apotex has paid its testifying experts more than $250,000.)

I would have been more impressed by Lee's testifying to the result of his or his team's doing a Raman scan of the Apotex samples than I was by Batchelder's testimony. I was additionally troubled to learn that of the three Raman experts whom SmithKline considered for hiring to be an expert witness, the two who were turned down in favor of Batchelder had extensive experience in Raman microscopy of drug compounds. Batchelder had virtually none, which is why he required a tutorial by Dr. Lee.

Although witness after witness testified to the importance of doing multiple tests on the same sample because of the potential for error and ambiguity in tests of crystal structure, no sample of Apotex's product was tested both by PLS-enhanced spectroscopy and Raman microscopy. Nor did Niemczyk or Batchelder test all the samples of Apotex product that SmithKline had obtained in discovery. Although I specifically asked SmithKline how many samples had been obtained from Apotex and how many of them had been tested by Niemczyk or Batchelder, I never received a satisfactory answer. As near as I can determine, Niemczyk tested 9 out of 52 samples of bulk material and Batchelder 16 out of 29 batches of pills. The pill batches, however, sometimes consisted of more than one bottle of pills and I have no idea how many pills in all were produced to SmithKline and why Batchelder singled out certain of them but not others for testing. Moreover, for unexplained reasons he did many more scans of some pills than of others. Also unexplained is why he did edge scans of some pills but not of others.

It was also never explained at trial why Niemczyk tested just bulk material and Batchelder just pills. In its post-trial brief, SmithKline, without record references, says that Niemczyk was given bulk material to test because his methodology was an excellent one for bulk material and had been used in a previous patent case of SmithKline's, involving a different drug, on bulk material, while Batchelder was

given tablets because Raman microscope can do edges. Neither proposition, even if credited despite the absence of record support (as I am disinclined to do, for it was a question I had put to SmithKline early in the trial), suggests that Raman cannot be done effectively on bulk material or PLS effectively on tablets.

For all these reasons, taken together, I apply a sharp discount factor to both Niemczyk's and Batchelder's testimony. Indeed, I might well have been justified in excluding their testimony altogether under the standard of *Daubert v. Merrell Dow Pharmaceuticals, Inc.*, 509 U.S. 579, 113 S.Ct. 2786, 125 L.Ed.2d 469 (1993); see also Fed.R.Evid. 702, as urged by Apotex, on the ground that these two scientists did not do their work for SmithKline in this litigation with the same rigor with which they do their academic work. *Kumho Tire Co. v. Carmichael*, 526 U.S. 137, 152, 119 S.Ct. 1167, 143 L.Ed.2d 238 (1999); *Sheehan v. Daily Racing Form, Inc.*, 104 F.3d 940, 942 (7th Cir.1997); *Cummins v. Lyle Industries*, 93 F.3d 362, 369 (7th Cir.1996). This by the way is another issue controlled by regional, not Federal Circuit, procedural law, *Micro Chemical, Inc. v. Lextron, Inc.*, 317 F.3d 1387, 1390-91 (Fed.Cir.2003), though with respect to the *Daubert* issue the distinction is not important because Seventh Circuit law tracks the Supreme Court's authoritative pronouncements, as of course Federal Circuit law does as well.

The primary purpose of the *Daubert* filter is to protect juries from being bamboozled by technical evidence of dubious merit, *Seaboard Lumber Co. v. United States*, 308 F.3d 1283, 1301-02 (Fed.Cir.2002), as is implicit in the courts' insistence that the *Daubert* inquiry performs a "gatekeeper" function. E.g., *Smith v. Ford Motor Co.*, 215 F.3d 713, 718 (7th Cir.2000). In a bench trial it is an acceptable alternative to admit evidence of borderline admissibility and give it the (slight) weight to which it is entitled. The

Federal Circuit in *Seaboard Lumber Co. v. United States*, *supra*, 308 F.3d at 1302, while pointing to the concern with protecting juries from confusion, did say that the *Daubert* standard must be followed in bench trials as well. But it did not say that it must be followed *rigidly* in such trials. *Daubert* requires a binary choice—admit or exclude—and a judge in a bench trial should have discretion to admit questionable technical evidence, though of course he must not give it more weight than it deserves. This at any rate was my approach with respect to Niemczyk and Batchelder, and I do not consider their evidence to have been wholly lacking in credibility or probative value. While the sum of zero plus zero is zero, the sum of one plus one is two; and the convergent result of two weak tests is more robust than the result of each test taken in isolation; so maybe one plus one is three. But if proof by a preponderance of the evidence is modeled as scoring 5.01 points out of 10, then 3 out of 10 won't hack it.

This cannot conclude the analysis, because of the evidence discussed earlier concerning the tests that BCI conducted on its product, and because of testimony by Dr. Byrn that with proper methods Apotex could probably keep the amount of hemihydrate in its product down to the 2 to 4 percent range. The implication is that even if Niemczyk and Batchelder failed to detect hemihydrate, the methods they used could have done so; and just as existence and detection are not the same thing, neither are detectability and detection. Still, the unimpressive showing by Niemczyk and Batchelder, both skilled practitioners of their respective methods for detecting minute percentages of a polymorph in a mixture with another polymorph, leaves me highly skeptical. My doubts are enhanced by the profound scientific uncertainty concerning the mechanism and precise effects of adventitious seeding both in general and specifically with respect to paroxetine hydrochloride hemihydrate, by the fact that I am making a predictive judgment, and by the fact that the other evidence of

conversion, designed to bolster Niemczyk and Batchelder, is, as I discussed earlier, very weak. Although I regard the question as a close one, I conclude that SmithKline has failed to prove by a preponderance of the evidence that Apotex is likely to produce a product that contains enough hemihydrate to be detectable even by PLS or Raman.

Only if the "single crystal" interpretation of claim 1 is correct, therefore, has SmithKline proved infringement. But if that interpretation is correct, the patent is invalid for indefiniteness.

Seeding as an Equitable Defense

But now suppose all this is wrong and SmithKline *has* proved infringement of a valid claim 1. It must still lose this case, for two independent reasons both rooted in equity. Equity figures in two fundamental ways in law. First, it is a source of defenses to liability—in patent as in other cases, as illustrated by the well-known defense of prosecution-history estoppel. *Festo Corp. v. Shoketsu Kinzoku Kogyo Kabushiki Co.*, 535 U.S. 722, 122 S.Ct. 1831, 152 L.Ed.2d 944 (2002). Second, it furnishes the norms that guide the grant or denial of equitable relief. Both figure here. But before proceeding further I must emphasize that in referring to "equity" I am referring not to some vague sense of "fairness" but to the body of principles that has crystallized (pardon the pun) over centuries of Anglo-American jurisprudence and become a part of patent law as of the other fields of American law.

Although I cannot find any statutory language or case law that bears on the question, I believe that as a matter of fundamental principle it must be a defense to a charge of patent infringement that the patentee caused the infringement. There are many analogies, but one will suffice: it is a completely orthodox defense to a suit for breach of contract that the plaintiff prevented the defendant from performing his contractual duty. See, e.g., *Zobel & Dahl Construction v.*

Crotty, 356 N.W.2d 42, 45 (Minn.1984); *Pfaff v. Petrie*, 396 Ill. 44, 71 N.E.2d 345, 351 (1947); *Chicago Title & Trust Co. v. Hedges Mfg. Co.*, 91 Ill.App.3d 173, 46 Ill.Dec. 510, 414 N.E.2d 232, 236-37 (1980). Had SmithKline snuck into BCI's plant and scattered hemihydrate seeds, I do not think that even SmithKline would deny that Apotex would have a good defense to a claim of infringement of patent 723.

Of course, SmithKline did not do that. It did not deliberately seed BCI's plant. And no evidence was presented as to whether Apotex could have made the hemihydrate that it produced in the course of development of its anhydrous paroxetine product in some other facility, which would then no doubt become seeded but could be abandoned or diverted to another product and the anhydrate be produced at BCI's virginal facility. But would it remain virginal? Quite possibly not, since some of the personnel involved in the experimental preparations at the remote facility would have occasion to visit BCI and there would be no way to disinfect them of seeds before the visit. Remember ritonavir. Remember too that Apotex was within its rights in making hemihydrate for experimental purposes because the Hatch-Waxman Act allows manufacturers to experiment with a patented drug while developing its generic equivalent.

SmithKline urged repeatedly throughout the trial that while seeds are not necessary to produce paroxetine hydrochloride hemihydrate, they are necessary for the conversion of anhydrate to hemihydrate. If there are seeds in BCI's plant, how did they get there? There are only two possibilities consistent with the trial record. The first is that they wafted there from SmithKline. The second is that they were produced when Apotex made hemihydrate as part of its developmental process. That was not infringement; that was a licensed use, licensed by virtue of the Hatch-Waxman Act, of SmithKline's property right. The ultimate responsibility for the seeding of BCI's plant was SmithKline's.

SmithKline harped incessantly at the trial on the fact that Apotex applies an aqueous coating to its anhydrate pills rather than a nonaqueous coating, such as shellac. But the head of TorPharm (remember it is TorPharm that makes the pills out of the bulk material that it receives from BCI) testified without contradiction that the U.S. and Canadian regulatory authorities discourage the use of the nonaqueous coatings on pills. So it seems that on SmithKline's theory of infringement, between governme: and SmithKline generic producers are disabled from producing a public-domain product however strenuous the efforts they make to avoid committing a purely nominal infringement.

SmithKline goes so far as to argue that what prevented Apotex from manufacturing a stable anhydrate, that is, one that would not convert to hemihydrate if seeded, is that SmithKline had obtained a patent on the stable anhydrate (Form C). And this flags a more general concern. According to sources discussed in Bernstein, *supra*, at 11-12, the more money that is spent looking for polymorphs, the more polymorphs are found. As a result, the pharmaceutical industry sees more than its share of polymorph discoveries. We know from Ostwald's Rule that later-discovered polymorphs tend to be more stable than the earlier ones. Just as SmithKline argues that Apotex's anhydrate converts to hemihydrate, hemihydrate itself may convert to a new, more stable form of anhydrate discovered and patented by SmithKline, resulting in the indefinite extension of what is in effect Ferrosan's discovery in the 1970s of paroxetine. Patent 723 will expire in three and a half years. But SmithKline's patent on Form C will not expire until 2016 at the earliest, 39 years after Ferrosan obtained patent 196.

To repeat an earlier point, Apotex gains nothing from the seeding of its plant. As Dr. Batchelder put it, if you are trying to make anhydrate, any hemihydrate that gets into it is an impurity. The effect of seeding is to impose on Apotex

additional costs of production as it makes efforts, probably, as I have said, in vain, to purge its production process of hemihydrate seeds. Apotex is not appropriating value that belongs to SmithKline by virtue of patent 723, because it is incurring costs rather than reaping any benefits from the fact that BCI's plant is seeded and therefore some of its anhydrate may convert to hemihydrate. The only possible effect of preventing the alleged infringement would be to perpetuate an expired patent (patent 196, which expired more than a decade ago) by making it impossible for Apotex to manufacture a formerly patented substance that is now in the public domain. That would be true even if, to recur to an earlier example, Apotex had spent a billion dollars to purge BCI's plant of hemihydrate seeds. The purging would probably fail (remember that a seed might be as small as 10 molecules); and the expenditure on the attempt would have no social product and should not be encouraged.

The case for Apotex's having an affirmative defense to infringement is stronger the broader the interpretation of claim 1. Apotex has taken steps to avoid producing hemihydrate in amounts detectable under traditional measures with their 5 to 8 percent limit of detection, and SmithKline itself argues that by heroic means Apotex could even get below the limits of detection by PLS and Raman microscopy. But Apotex cannot eliminate *all* crystals of hemihydrate; under a single-crystal interpretation of claim 1, SmithKline is the sole cause of infringement.

Mention of equitable defenses to patent infringement brings to mind the Federal Circuit's statement of just two months ago concerning the reverse doctrine of equivalents, "under which an accused product or process that falls within the literal words of a claim nevertheless may not infringe if the product or process 'is so far changed in principle from a patented article that it performs the same or a similar function in a substantially different way.' *Graver Tank & Mfg. Co. v.*

Linde Air Prod. Co., 339 U.S. 605, 608-09, 70 S.Ct. 854, 94 L.Ed. 1097 (1950); see generally Donald S. Chisum, 5A *Chisum on Patents* § 18.04 (1999). This doctrine is equitably applied based upon underlying questions of fact, see *Scripps Clinic & Research Foundation v. Genentech, Inc.*, 927 F.2d 1565, 1581 (Fed.Cir.1991), when the accused infringer proves that, despite the asserted claims literally reading on the accused device, 'it has been so changed that it is no longer the same invention.' *Del Mar Avionics, Inc. v. Quinton Instr. Co.*, 836 F.2d 1320, 1325 (Fed.Cir.1987) (citing *Graver Tank*, 339 U.S. at 608-09, 70 S.Ct. 854)." *Amgen Inc. v. Hoechst Marion Roussel, Inc.*, 314 F.3d 1313, 1351 (Fed.Cir.2003).

The defense failed in *Amgen*. The court was "not persuaded by TKT that this is a case where equity commands a determination of non-infringement despite its product literally falling within the scope of the asserted claims." *Id.* But what is more important is the court's recognition that there might be a case "where equity commands a determination of non-infringement despite its product literally falling within the scope of the asserted claims." This is a pretty good description of the present case, though since Apotex did not invoke the reverse doctrine of equivalents I do not rely on it. This is a case in which the patented product on which the claim of infringement is based has been so changed that it is no longer the same invention. The hemihydrate that is found in small quantities in the anhydrate is not the same invention covered by patent 723; it is merely an impurity.

Equitable Limitations on Patentee Relief

But suppose this too is wrong, and Apotex is guilty of infringement and has no defenses. The next and last question I need consider is relief. The relief sought by SmithKline, apart from attorney's fees on the ground that Apotex's infringement was willful, is twofold: an injunction against Apotex's producing the anhydrate until patent 723 expires and an order, authorized by the Hatch-Waxman Act, in effect

directing the FDA to delay its granting Apotex's ANDA until patent 723 expires, an order that would have the same effect as the injunction.

The grant of an injunction in the circumstances disclosed by the evidence in this case would be a travesty of equity. An injunction is a substitute for an award of damages in situations in which damages are difficult to calculate or are otherwise inadequate as a remedy for the wrong done by the defendant to the plaintiff. *Walgreen Co. v. Sara Creek Property Co., B.V.*, 966 F.2d 273, 274-76 (7th Cir.1992); *Ocean Spray Cranberries, Inc. v. PepsiCo, Inc.*, 160 F.3d 58, 61 (1st Cir.1998). It is not to provide relief when damages are known to be zero. To provide relief in such a case would be to invite a form of extortion. *Marseilles Hydro Power, LLC v. Marseilles Land & Water Co.*, 299 F.3d 643, 651 (7th Cir.2002); *Youngs v. Old Ben Coal Co.*, 243 F.3d 387, 393 (7th Cir.2001). A plaintiff who told a court that he wanted an injunction *because* he had not sustained and did not expect to sustain any damages whatsoever, but that naturally he wanted *something* to show for the bother of having sued and the something he wanted was an injunction that he could use to extract a licensing fee, would be thrown out of court on his ear. But consider what damages SmithKline might seek in the event that Apotex is permitted to produce and sell its anhydrate and the anhydrate is discovered to contain 2 percent (or perhaps 5 or even 10 percent-i.e., well short of "high double digits") hemihydrate. "Damages is the amount of loss to a patentee." *SmithKline Diagnostics, Inc. v. Helena Laboratories Corp.*, 926 F.2d 1161, 1164 (Fed.Cir.1991). Since the hemihydrate in Apotex's product would not be replacing any hemihydrate sold by SmithKline or (until it reached the high double digits, which has not been proved to be likely) doing anything for Apotex that might give it a competitive advantage that would inflict a loss on SmithKline, SmithKline would have no lost profits; its damages would be zero.

Against this SmithKline argues that it would suffer a loss measured by the diminution in its profits from Paxil as a result of competition from Apotex's anhydrate, which has the same therapeutic benefit as Paxil. But a patentee will not be heard to complain of losses that are due to competition from a product that is in the public domain. (Of course I am assuming as I must that Apotex won't be infringing an anhydrate patent of SmithKline's; that is the issue in other litigation.) The implication of such a complaint would be that patents should last forever and generic equivalents be outlawed. The engine of the competition that SmithKline fears is not the 2 or 5 or 10 percent hemihydrate in Apotex's product, if that is what there is going to be, but the 98 or 95 or 90 percent anhydrate; for Apotex's competition would not be less effective if the product were 100 percent anhydrate.

Another way to explain SmithKline's disentitlement to an injunction is in terms of the doctrine, classically equitable—an aspect of the historic doctrine of "unclean hands"—of patent misuse. *C.R. Bard, Inc. v. M3 Systems, Inc., supra*, 157 F.3d at 1372. The core of that doctrine is the proposition that a patent may not be used to obtain more protection from competition than patent law contemplates. The doctrine is defined in and illustrated by *Morton Salt Co. v. G.S. Suppiger Co.*, 314 U.S. 488, 491-93, 62 S.Ct. 402, 86 L.Ed. 363 (1942), where we read that "the use of [a patent] to suppress competition in the sale of an unpatented article may deprive the patentee of the aid of a court of equity to restrain an alleged infringement by one who is a competitor." *Id.* at 491, 62 S.Ct. 402. The patentee of a machine for processing salt required its customers to buy the salt for use in the machine from the patentee as well. This was held to be patent misuse. The example is archaic and the outcome wrong (and now largely superseded, see 35 U.S.C. § 271(d)(5)), because "tying" an unpatented to a patented product is not, as was believed when *Morton Salt* was decided, an effective method of extending the patent monopoly. Cf. *In re Independent*

Service Organizations Antitrust Litigation, 203 F.3d 1322, 1326-27 (Fed.Cir.2000). The machine and the salt were complements, in the economic sense that two products are complements if an increase in the price of one causes a reduction in the demand for the other. If the patentee refused to license its machine unless the licensee paid him a monopoly price for the salt that he needed if he was to obtain any benefit from using the machine, the patentee could not charge as much for the license. See, e.g., *Scheiber v. Dolby Laboratories, Inc.*, 293 F.3d 1014 (7th Cir.2002).

The present case illustrates, in contrast to *Morton Salt* and other tying cases, the economically *rational* use of a patent to obtain patent protection beyond the contemplation of patent law. Cf. *Symbol Technologies, Inc. v. Opticon, Inc.*, 935 F.2d 1569, 1581 (Fed.Cir.1991) ("double patenting" doctrine). SmithKline owned a patent on anhydrous paroxetine that expired in 1992. At that point anhydrous paroxetine entered the public domain and any firm that could satisfy the FDA that its anhydrate was bioequivalent to SmithKline's hemihydrate approved by the FDA that year for sale to the public could compete with SmithKline as soon as the FDA's five-year embargo on the sale of a bioequivalent of a new chemical entity ended. (It was only later that SmithKline muddied the waters by obtaining additional paroxetine patents.) Were SmithKline to obtain an injunction against Apotex's producing and selling its anhydrous Paxil substitute, it would be as if the original patent, 196, had not expired in 1992 but instead will not expire until 2006. SmithKline will have gained a 14-year extension of the patent term without authorization in the patent statute. Maybe the statutory term of drug patents is too short, as SmithKline argued in one of its filings in this case, but that is a complaint to be made to Congress rather than to the courts.

By no means do I advocate making "patent misuse" a general equity solvent for "sympathetic" cases. See *C.R.*

Bard, Inc. v. M3 Systems, Inc., supra, 157 F.3d at 1373. I have written against that misuse of misuse, *USM Corp. v. SPS Technologies, Inc.*, 694 F.2d 505, 510-12 (7th Cir.1982), as have the Supreme Court and other courts against parallel proposals to subordinate bankruptcy law to vague equitable standards. *Butner v. United States*, 440 U.S. 48, 55-56, 99 S.Ct. 914, 59 L.Ed.2d 136 (1979); *In re Stoecker*, 179 F.3d 546, 551 (7th Cir.1999); *In re Ludlow Hospital Society, Inc.*, 124 F.3d 22, 27 (1st Cir.1997). It does not follow that patent misuse is a closed category. When the advance of science well illustrated by the products in this case enables a form of patent misuse that is new but is well within the conceptual heartland of the doctrine, the boundaries of the doctrine can expand modestly to encompass it. "The sea-changes in both law and technology stand as a testament to the ability of law to adapt to new and innovative concepts, while remaining true to basic principles." *AT&T Corp. v. Excel Communications, Inc.*, 172 F.3d 1352, 1356 (Fed.Cir.1999). It would be inappropriate to confine patent misuse, as is sometimes suggested, to practices that violate antitrust law, for in that event the doctrine would be superfluous.

But mention of antitrust serves to bring to mind the close analogy between the form of patent misuse that I am exploring and the doctrine of "antitrust injury." *Brunswick Corp. v. Pueblo Bowl-O-Mat, Inc.*, 429 U.S. 477, 486-88, 97 S.Ct. 690, 50 L.Ed.2d 701 (1977); *Atlantic Richfield Co. v. USA Petroleum Co.*, 495 U.S. 328, 337, 339, 110 S.Ct. 1884, 109 L.Ed.2d 333 (1990); *Dial A Car, Inc. v. Transportation, Inc.*, 82 F.3d 484, 486-87 (D.C.Cir.1996). Suppose that two competing firms merge in violation of antitrust law, but so efficient is the merger that the effect of eliminating competition between the merging firms on the market price (maybe they have so large a share of the market that jointly they enjoy a practical monopoly) is dominated by the effect of the merger in reducing the costs of the firm resulting from the merger, compared to the costs of the predecessor firms;

and in consequence the firm reduces its price below the old competitive price. This is not a fanciful example; if a monopolist's costs are much lower than those of the competitive industry that it has replaced, it is entirely possible that the optimal monopoly price will lie below the former competitive price. The remaining firms in the market must now lower their price in order to remain competitive, and so they are injured. But the injury is not actionable, as *Brunswick* and subsequent cases make clear. It is not "antitrust injury" (that is, injury for which antitrust law provides a remedy) because it is not the sort of injury that antitrust seeks to remedy.

Likewise any injury that SmithKline sustains from the fact that minute amounts of its product creep into Apotex's generic product will be due not to the invasion of any interest that patent law protects, but merely to the fact that the existence of a public-domain substitute for a patented product injures the patentee by providing competition. Again, at the risk of tedious repetition, the efficacy of Apotex's generic competition with Paxil will gain nothing from the fact that Apotex cannot eliminate minuscule quantities of the hemihydrate from its anhydrate product. The infiltration of Apotex's production process by hemihydrate is merely a pretext for an infringement suit designed to prevent competition from a product that is in the public domain. It is like the complaint of the fringe firms in my merger example about having to compete with a firm that has lower costs.

The doctrine of antitrust injury is not esoteric but instead illustrates the general principle that causation in the legal sense requires that the injury to the plaintiff be the kind of injury that the law that the defendant violated was intended to prevent. The principle is illustrated by the colorful though very sad old case of *Gorris v. Scott*, 9 L.R.-Ex. 125 (1874). The plaintiff's animals, while being transported on the deck of defendant's ship, lost their footing and were swept over-

board in a storm. The ship was not equipped with pens required by statute to prevent the spread of disease among the animals. Had there been pens, the animals would not have been washed overboard. But the plaintiff lost the case because the statute was not aimed at preventing that type of injury. See *Jack Walters & Sons Corp. v. Morton Bldg., Inc.*, 737 F.2d 698, 708-09 (7th Cir.1984); W. Page Keeton *et al.*, *Prosser & Keeton on the Law of Torts*, § 36, pp. 222-26 (5th ed.1984). The principle is general and I cannot think of any reason why it should not apply to patent law, although I have found only one opinion that endorses the principle, and that a dissent, *Rite-Hite Corp. v. Kelley Co.*, 56 F.3d 1538, 1558-60, 1575 (Fed.Cir.1995) (en banc)—but the majority did not reject (or endorse) the principle.

SmithKline acknowledges as it must the applicability of equitable principles to the grant of injunctions in patent cases, 35 U.S.C. § 283; *Rite-Hite Corp. v. Kelley Co., Inc., supra*, 56 F.3d at 1547-48, and complains about their application to its request for an injunction (should I find as I have that it has failed to prove that Apotex's product will contain more than infinitesimal amounts of the hemihydrate) only on the inadmissible ground that Congress has not made the statutory term of drug patents long enough. But it denies that the alternative remedy that it seeks under the Hatch-Waxman Act is subject to equitable principles. The principal argument that it makes in support of this distinction (which it actually forgot in a portion of its post-trial brief in which it stated that in the case of "single crystal" infringement "it would be unlikely that a court would grant injunctive relief *or anything* other than nominal damages" (emphasis added)) is that the erasure of equitable principles was part of the quid pro quo for the right of experimental use that the Act granted the generic manufacturers.

I am troubled not by the novelty of the argument but by the lack of evidence to support it. The patentee's quid for the

generic manufacturer's quo in the Hatch-Waxman Act was the extension of the patent term while the patentee was seeking the FDA's approval to market the patented drug, 35 U.S.C. § 156(c), plus the mandatory 30-month stay of FDA approval if the patentee sued a generic manufacturer for infringement. 21 U.S.C. § 355(j)(5)(B)(iii). See, e.g., *Warner-Lambert Co. v. Apotex Corp., supra*, 316 F.3d at 1357; H.R.Rep. No. 857 (Part I), 98th Cong., 2d Sess. 14-15 (1984); H.R.Rep. No. 857 (Part II), 98th Cong., 2d Sess. 11 (1984), U.S.Code Cong. & Admin.News 1984, p. 2686; Kristin E. Behrendt, "The Hatch-Waxman Act: Balancing Competing Interests or Survival of the Fittest?" 57 *Food & Drug L.J.* 247, 270 (2002). If the kind of hypertechnical infringement involved in this case (assuming that there is infringement at all, which I have found there is not) does not justify the issuance of an injunction—if indeed such issuance would ratify patent misuse directed against the manufacturers of generic drugs—what sense would it make to hold that the Hatch-Waxman Act, the main purpose of which was to facilitate competition from those manufacturers, entitles the patentee to precisely that inequitable remedy? It would make no sense. It would be a judicial amendment motivated by sympathy for SmithKline's argument that the patent term is too short for drugs. The Federal Circuit has held that in a case governed by the Hatch-Waxman Act "the substantive determination whether actual infringement or inducement will take place is determined by traditional patent infringement analysis, just the same as it is in other infringement suits, including those in a non-ANDA context, the *only* difference being that the inquiries now are hypothetical because the allegedly infringing product has not yet been marketed." *Warner-Lambert Co. v. Apotex Corp., supra*, 316 F.3d at 1365-66 (emphasis added). Under "traditional patent infringement analysis," SmithKline is not entitled to an injunction; so neither is it entitled to an order forbidding the FDA to approve Apotex's ANDA.

I am mindful that the Act uses "shall" rather than "may" language in reference to postponing the entry of the generic drug into the market, 35 U.S.C. § 271(e)(4)(A) ("the court shall order the effective date of any approval of the drug . . . involved in the infringement to be a date which is not earlier than the date of the expiration of the patent which has been infringed"), whereas the patent statute states that "courts having jurisdiction of cases under this title may grant injunctions in accordance with the principles of equity." 35 U.S.C. § 283. But "shall versus may" arguments are weak in general and in this case. As the Supreme Court noted in *Gutierrez de Martinez v. Lamagno*, 515 U.S. 417, 432 n. 9, 115 S.Ct. 2227, 132 L.Ed.2d 375 (1995), "Though 'shall' generally means 'must,' legal writers sometimes use, or misuse, 'shall' to mean 'should,' 'will,' or even 'may.' See D. Mellinkoff, *Mellinkoff's Dictionary of American Legal Usage* 402-403 (1992) ('shall' and 'may' are 'frequently treated as synonyms' and their meaning depends on context); B. Garner, *Dictionary of Modern Legal Usage* 939 (2d ed. 1995) ('[C]ourts in virtually every English-speaking jurisdiction have held—by necessity that—*shall* means *may* in some contexts, and vice versa.'). For example, certain of the Federal Rules use the word 'shall' to authorize, but not to require, judicial action. See, e.g., Fed. Rule Civ. Proc. 16(e) ('The order following a final pretrial conference *shall* be modified only to prevent manifest injustice.') (emphasis added); Fed. Rule Crim. Proc. 11(b) (A *nolo contendere* plea '*shall* be accepted by the court only after due consideration of the views of the parties and the interest of the public in the effective administration of justice.') (emphasis added)." See also *Gray-Bey v. United States*, 201 F.3d 866, 867-70 (7th Cir.2000).

In this case the natural explanation for the different usages has nothing to do with quids or quos. In the ordinary case of patent infringement, the infringement has already occurred and so damages are a possible remedy, and in deciding

whether to grant an injunction the judge must weigh the pros and cons of the alternatives in the setting of the particular case. But the Hatch-Waxman order comes before any actual infringement, so there is no possible alternative remedy of damages (there is the possibility of an injunction against the infringer to back up the delay order, and that is authorized by section 271(e)(4)(B)). Section § 271(e)(4)(C) is explicit that the court may not award damages unless the infringer has begun commercial production or importation, that is, has begun competing with and therefore inflicting losses on the patentee, and so there cannot be a damages award in a case such as the present one. In a case such as this it is the order or nothing. The only relief possible is equitable. If equity requires in such an unusual case that the equitable relief sought be nothing, I cannot think of any reason for casting equity aside.

So the Supreme Court held in another "shall" case, *Hecht Co. v. Bowles*, 321 U.S. 321, 64 S.Ct. 587, 88 L.Ed. 754 (1944). The Emergency Price Control Act of 1942 provided that if the administrator of the Act showed that a person had violated it, an injunction or other order "shall be granted" by the court to which the administrator applied for relief. Yet the Court held that the court retained discretion to withhold relief in an appropriate case. A similar case is *Robbins v. McNicholas Transportation Co.*, 819 F.2d 682, 684-86 (7th Cir.1987). The present case is stronger than either of these for softening the imperative force of "shall." Had Congress said "the court *may* order the effective date of any approval of the drug . . . involved in the infringement to be a date which is not earlier than the date of the expiration of the patent which has been infringed," it would have caused a good deal of judicial head-scratching. Judges would have wondered what on earth Congress had been thinking of when it said "may" rather than "shall." It could not have been thinking about this case, unforeseen in 1984. I am not aware of any case before the present one in which the judge would have

been warranted in withholding the delay order after finding infringement. Congress has neither the leisure nor the foresight (it would have to be omniscient) to provide an answer for every question that might arise in a case governed by one of its statutes. It enacts statutes against a background of legal understandings that inform the decision of unforeseen cases, and that include the principles of equity. Section 271(e)(4)(A) is an amendment to the patent statute and it provides relief in the nature of an injunction, for an injunction is simply a court order (other than a purely procedural one) to do or not to do something. As a form of patent injunction, the delay order is subject to the principles that govern such injunctions, although only in a very unusual case will those principles counsel for withholding relief. But this is the unusual case.

There is still another consideration. If Congress had wanted to extinguish judicial discretion to withhold the order postponing the entry of the generic drug, it could have done so very easily by providing not that "*the court shall order* the effective date of any approval of the drug . . . involved in the infringement to be a date which is not earlier than the date of the expiration of the patent which has been infringed" but instead that "the effective date of any approval of the drug . . . involved in the infringement *shall be* a date which is not earlier than the date of the expiration of the patent which has been infringed." Congress did not do that. That would have been like a law which says that a felon can't vote. The court decides whether the defendant committed a felony, but if it decides that he did, then the disqualification (corresponding to the postponement of the entry of the generic drug into the market) attaches automatically, without judicial intermediation. But here, instead of attaching a disqualification or other sanction automatically to an adjudicated infringer, Congress interposed the court between the statute and its application in an individual case by requiring that the order come from the court. No purpose would be served by such

interposition if the court could never, no matter what the circumstances—however remote from anything contemplated by Congress—refuse to issue the order once infringement had been established.

So SmithKline is entitled to no relief—but not because if there was infringement it was *de minimis*. Whether there is a *de minimis* defense in patent law is an unsettled question. *Glaxo, Inc. v. Novopharm, Ltd.*, 110 F.3d 1562, 1565-66 and n. 1 (Fed.Cir.1997). Clearly there is no such defense in general, because that would amount to a license to steal. E.g., *Pile v. Pedrick*, 167 Pa. 296, 31 A. 646 (1895). That is why the defense is rejected in cases that involve intentional torts, such as conversion. *Hessel v. O'Hearn*, 977 F.2d 299, 303-04 (7th Cir.1992). Patent infringement can be inadvertent as well as deliberate, as this case dramatically illustrates, but often it is deliberate and in such cases a *de minimis* defense would be unsound. The fair use defense of copyright law has a *de minimis* component, as where a writer copies a brief passage from a copyrighted work, but the reason is that since the brief passage is not a substitute for the copyrighted work but if anything an advertisement for it, the copyright holder could be expected to grant a license without demanding a fee, if a transaction were feasible, which it is not because of the stakes are so trivial. *Ty, Inc. v. Publications Int'l Ltd.*, 292 F.3d 512, 517-18 (7th Cir.2002).

The reason for excusing the alleged infringement in this case is not that Apotex stole only a little hemihydrate from SmithKline. It stole nothing from SmithKline. It doesn't *want* hemihydrate, and it derives no value from the hemihydrate that it unavoidably creates and "sells." If it made hemihydrate deliberately, or if it took advantage of 100 percent conversion to obtain a product that had hemihydrate's superior handling characteristics, that would be theft and it would be nonsense to point out that paroxetine is only 10 percent of the pill by weight. But if the person sitting next to

me at dinner spills his soup on my sleeve, I am not a thief even though I cannot remove the stain.

The distinction between the present case and a "pure" *de minimis* case is made clear in Judge Learned Hand's opinion in *Condenser Corp. v. Micamold Radio Corp.*, 145 F.2d 878, 880 (2d Cir.1944) (citations omitted), where he said that "we will not enjoin the defendant's machine for a detail, obviously so useless in function. Moreover, it would be equally unwarranted to give judgment for damages or profits; for it is inconceivable that the infringement, if there is any at all, . . . could add a cent to the defendant's profits, or could interfere in the slightest degree with the plaintiff's sales." See also *Pratt v. United States*, 95 Ct.Cl. 608, 43 F.Supp. 461, 475-76 (1942). Cf. *Kaz Mfg. Co. v. Chesebrough-Ponds, Inc.*, 317 F.2d 679, 680-81 (2d Cir.1963): "one who constructs a patented wall safe but uses it only as an anchor for his boat would not be a patent infringer since such use would not be for the purpose of utilizing the teachings of the patent." *Id.* at n. 3.

SmithKline points out that Apotex wants to take a free ride ("usurping," SmithKline calls it) on the considerable investment made by SmithKline in obtaining FDA approval for Paxil. It is indeed much easier to establish bioequivalence than it is to convince the FDA that an original drug is safe and effective. But that kind of free riding the law permits, and indeed the Hatch-Waxman Act encourages. Moreover, free riding is an integral part of the scheme of the patent law. In exchange for the exclusive and in the case of Paxil very valuable rights that a valid patent grants, the patentee is required to make public disclosure of the steps required to create the patented product, so that when the patent expires and the patented product enters the public domain competitors can manufacture the product. Those competitors are free riders with a vengeance. But they are lawful free riders. And so is Apotex.

To summarize:

I construe claim 1 of SmithKline's patent 723 to cover crystalline paroxetine hydrochloride hemihydrate in any commercially significant quantity, and so construed the claim is valid against the various attacks on it made by Apotex but clearly will not be infringed by Apotex's anhydrate product. I hold that if claim 1 is construed to claim single crystals of crystalline paroxetine hydrochloride hemihydrate, it is infringed, but that if the claim were so construed it would be invalid because of indefiniteness.

If claim 1 is construed to claim crystalline paroxetine hydrochloride hemihydrate in amounts detectable by means that existed when the patent was applied for or issued, I find that SmithKline has failed to prove by a preponderance of the evidence that Apotex's product will infringe claim 1.

I reach the same conclusion (though with less confidence) if claim 1 is construed to claim crystalline paroxetine hydrochloride hemihydrate in amounts detectable by any means. So construed, the claim might fail for indefiniteness, but I do not reach that question.

If contrary to the above, claim 1 is valid and will be infringed either by a single crystal of hemihydrate or by a barely detectable amount of it, Apotex has a complete affirmative defense that SmithKline is the cause of the infringement.

If claim 1 is valid and will be infringed and Apotex has no defense to liability, I hold that SmithKline nevertheless is entitled to no relief: neither an injunction against Apotex's making its anhydrate product nor an order based on the Hatch-Waxman Act delaying Apotex's sale of its anhydrate product until patent 723 expires. The grant of injunctive relief, whether under the patent statute or under the Hatch-Waxman Act, would be contrary to the principles of equity. SmithKline acknowledges the application of those principles

to its request for an injunction, and I hold that they also apply to its request for the delay order that would have the identical effect as the injunction.

For these reasons I am instructing the clerk of the district court to enter a final judgment for the defendants, dismissing SmithKline's suit with prejudice.

APPENDIX E

UNITED STATES DISTRICT COURT, N.D. ILLINOIS, EASTERN DIVISION.

No. 98 C 3852.

SMITHKLINE BEECHAM CORPORATION and Beecham Group, p.l.c.,
Plaintiffs,

v.

APOTEX CORP., Apotex, Inc., and TorPharm, Inc.,
Defendants.

July 17, 2002

MEMORANDUM OPINION

KOCORAS, Chief J.

Plaintiffs SmithKline Beecham Corporation and Beecham Group ("SmithKline") have filed four motions in limine; Defendants Apotex Corp., Apotex, Inc., and TorPharm, Inc. ("TorPharm") have filed seven. Decision of SmithKline's first motion in limine and TorPharm's second, fourth, sixth, and seventh motions is deferred until the time of trial, when we will entertain brief oral argument.

In their second motion in limine, SmithKline wishes to prevent TorPharm from introducing evidence bearing on the issue of invalidation of U.S. Letters Patent No. 4,721,723 ("the '723 patent") by public use. The motion encompasses testimony by Dr. William Wolf on that subject, both directly

and for rebuttal of testimony pertaining to patient use. Our November 30 opinion granted SmithKline summary judgment that the '723 patent was not invalid because of public use, obviating further attention to that issue at trial. TorPharm's opposition to the motion rests on the premise that we would reconsider our prior ruling. In light of the fact that we have declined to do so, SmithKline's argument that evidence bearing on the issue of public use, including Dr. Wolf's direct testimony, has no further purpose or place in this litigation. For reasons stated below, the testimony of Dr. Wolf will also be unnecessary for rebuttal of SmithKline's patient use evidence, so the second motion in limine is granted in its entirety.

SmithKline's third motion in limine revolves around TorPharm's efforts to invalidate the '723 patent under 35 U.S.C. § 112. Although TorPharm casts its argument in terms of § 112, this is nothing more than an effort to force SmithKline to use only the tests specifically enumerated in the language of the '723 patent to show the presence of infringing material within TorPharm's proposed product. Because our prior opinion already held that SmithKline is not so constrained, TorPharm's latest variation on this theme is just as unavailing as previous endeavors. Accordingly, SmithKline's motion to preclude TorPharm from advancing evidence of invalidation under § 112 is granted.

SmithKline's fourth motion in limine and TorPharm's third motion in limine are flip sides of the same coin. Both center on whether SmithKline can adduce evidence of the amount of hemihydrate present in TorPharm's product after it is marketed. TorPharm insists that we have already decided this issue in their favor, whereas SmithKline contends that no legal authority exists for the proposition that in cases brought under 35 U.S.C. § 271(e)(2)(A), an infringement analysis must focus on the state of the product at the time it is sold. On this issue, TorPharm has the better of this argument. The Federal

Circuit has explicitly stated that "[w]hat is likely to be sold, or, preferably, what will be sold, will ultimately determine whether infringement exists." *Glaxo, Inc. v. Novopharm, Ltd.*, 110 F.3d 1562, 1570 (Fed.Cir.1997); *see also Bayer AG. v. Biovail Corp.*, 279 F.3d 1340, 1346 (Fed.Cir.2002); *Bayer AG v. Elan Pharmaceutical Research Corp.*, 212 F.3d 1241, 1248 (Fed.Cir.2000); *Ben Venue Laboratories, Inc. v. Novartis Pharmaceutical Corp.*, 146 F.Supp.2d 572, 579-80 (D.N.J. 2001). The *Glaxo* court went on to note the importance of this time limitation in cases involving compounds that are capable of existing in various forms, such as the paroxetine hydrochloride at issue here. *Glaxo*, 110 F.3d at 1568. Changes that may occur in a product because of events that occur after the product is sold have no effect on the question of whether the "hypothetical" product at issue in an ANDA case will infringe at the time of sale, although they could come into play in deciding whether an actual commercial product infringes under § 271(a), a section not implicated in this case. *See Bayer*, 279 F.3d at 1350 ("infringement under § 271(e)(2)(A) by submission of an ANDA is not synonymous with infringement under § 271(a) by a commercial product").

SmithKline principally relies on *Bayer AG v. Biovail Corp.* to support its position that postsale events are fair game in an ANDA infringement action. 279 F.3d 1340. However, their reading of *Bayer* is much too expansive; in that case, the Federal Circuit held only that measurements taken both before and after manufacture of tablets were relevant to a § 271(e)(2)(A) analysis. Both of these events, however, take place *before* the product is marketed, and the *Bayer* court specifically stated that the inquiry must look to what will likely be marketed under the ANDA. *Bayer*, 279 F.3d at 1346; *see also id.* at 1349 (stating that measurements of actual materials, rather than what is described in the ANDA, is "at best, only tangentially relevant to an ANDA infringement analysis"). Other cases to which SmithKline points are inapposite in that they focus on actual infringement or other

patent-related issues, not the hypothetical scenario created by an ANDA submission. *See, e.g., Hoechst-Roussel Pharmaceuticals, Inc. v. Lehman*, 109 F.3d 756 (Fed.Cir.1997); *Zenith Laboratories, Inc. v. Bristol-Myers Squibb Co.*, 19 F.3d 1418 (Fed.Cir.1994). Furthermore, SmithKline's theory of inducement to infringe emerges from cases that involved patents claiming particular uses of a drug. The ANDAs filed in those cases did not include the claimed uses, but the drugs would be prescribed by physicians for the uses disclaimed by the ANDA and claimed by the patent. *See Bristol-Myers Squibb Co. v. Immunex Corp.*, 86 F.Supp.2d 447 (D.N.J. 2000); *Warner-Lambert Co. v. Apotex Corp.* 1999 WL 259946, at *3 (N.D.Ill. Apr.8, 1999). The courts faced with such situations held that the ANDA filer could be held liable for inducing the physicians to put the drugs to uses not covered by the ANDA and explicitly claimed in the pre-existing patents. The fact that those plaintiffs could proceed on an inducement theory does not make such a claim viable here; those cases are clearly factually distinguishable from the instant case. As such, they do not impact our conclusion that patient use evidence, because it involves changes to the state of the paroxetine hydrochloride after the product is sold, is not relevant to the question of whether the proposed compound will contain infringing material at the time it is sold. Consequently, TorPharm's motion to exclude this evidence is granted and SmithKline's motion to admit it is denied.

TorPharm's first motion in limine is related to the preceding discussion; they seek to prevent SmithKline from offering data obtained from expired tablets, tablets made from processes other than those given in the ANDA, and tablets made by its affiliates that will not be sold in the United States. For the reasons stated above, we agree that evidence derived from expired tablets is not relevant to the question of what will be sold. However, the latter two categories of evidence could bear on the qualities of the product TorPharm will ultimately market, and we are not limited to the four

corners of the ANDA in making that determination. *See Bayer,* 212 F.3d at 1248-49; *Glaxo,* 110 F.3d at 1568; *Abbott Laboratories v. Baxter Pharmaceutical Products, Inc.*, 2002 WL 449012, at *2. The motion is therefore granted with respect to tablets that have expired but otherwise denied.

Finally, TorPharm's fifth motion in limine attempts to preclude SmithKline from introducing any evidence derived from the commercial embodiment of the subject matter of the '723 patent. TorPharm is correct that an allegedly infringing product must be compared only to the claims of the patent, not the commercial embodiment manufactured by the patentee. *See Glaxo Group, Ltd. v. TorPharm, Inc.*, 153 F.3d 1366, 1373 (Fed.Cir.1998); *Zenith Laboratories, Inc. v. Bristol-Myers Squibb Co.*, 19 F.3d 1418, 1423 (Fed.Cir. 1994). However, the situation here is more subtle than TorPharm would make it out to be. The characteristic results from the testing methods that SmithKline seeks to use were not included in the language of the '723 patent. To obtain any basis for comparison, SmithKline identified a compound matching all of the characteristics listed within the patent and then used that compound to obtain reference data with the new testing methods. To adopt TorPharm's argument that this process amounts to an unacceptable comparison of their compound to the commercial embodiment of the patent would allow them to escape the effect of our prior decision that SmithKline may employ testing methods not enumerated within the language of the patent. As stated above, we will not allow them to circumvent that ruling. However, their point is well taken that the reference materials, to be an acceptable basis for a point of comparison, must exhibit each and every one of the characteristics of the hemihydrate listed in the patent. With that caveat, we conclude that TorPharm's fifth motion in limine must be denied.

CONCLUSION

For the foregoing reasons, SmithKline's second and third motions in limine are granted. Their fourth motion in limine is denied. TorPharm's third motion in limine is granted. Their first is granted in part and denied in part, and the fifth is denied. All remaining motions in limine will be decided at time of trial.

APPENDIX F

UNITED STATES DISTRICT COURT
NORTHERN DISTRICT OF ILLINOIS
EASTERN DIVISION

98 C 3952

SMITHKLINE BEECHAM, CORPORATION and
BEECHAM GROUP, p.l.c.,
Plaintiffs,

vs.

APOTEX CORP., APOTEX, INC., and TORPHARM, INC.,
Defendants.

MEMORANDUM OPINION

CHARLES P. KOCORAS, *District Judge*:

This matter is before the Court on motions for summary judgment regarding the validity of Plaintiffs' patent and non-infringement of that patent by Defendants' proposed drug. For the reasons set forth below, we deny the Defendants' motions. We grant the Plaintiffs' motions on the issue of invalidity under 35 U.S.C. § 102(b), (f), and (g).

BACKGROUND

In the 1970s, scientists at the Danish company of A/S Ferrosan ("Ferrosan") discovered a new class of chemical compounds, at least some of which were reported to selectively inhibit the reuptake of serotonin, a naturally occurring chemical in the brain. Several commercial antidepressants common at the time acted by inhibiting the neuronal reuptake

of serotonin, and Ferrosan determined in laboratory tests that the serotonin-uptake inhibitory activity of its new compounds was comparable to that exhibited by these existing anti-depressant drugs. Ferrosan then applied for, and on February 8, 1977, was assigned, U.S. Patent No. 4,007,196 ("the '196 patent"). (TP Ex. 4.[1]) The patent was entitled "4-PHENYLPIPERIDINE COMPOUNDS;" according to the abstract, it "relate[d] to new 3-substituted 1-alkyl-4-phenylpiperidines, being useful as antidepressant and anti-Parkinson agents, and to their production." (*Id.*)

One of the 3-substituted 1-alkyl-4-phenylpiperidine compounds created by Ferrosan was paroxetine. (SB Resp. ¶ 10.) Ferrosan lacked the financial resources to fully commercialize a paroxetine-based drug product (SB Resp. ¶ 31), and on or about July 31, 1980, it licensed its paroxetine technology to the U.K. company Beecham Group Limited ("Beecham"). (*Id.* ¶ 32; TP Exh. 20.) The license granted Beecham the exclusive right to make, have made, use and sell

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[1] The following abbreviations are used in citations throughout this opinion:

- "TP"—TorPharm's Local Rule 56.1(a)(3) Statement of Material Facts in Support of Its Motions for Summary Judgment
- "TP Exh."— TorPharm Exhibits
- "SB Resp."—SB's Response to TorPharm's Local Rule 56.1(a)(3) Statement of Material Facts
- "SB Resp. Exh."—Exhibits to SB's Response to TorPharm's Local Rule 56.1(a)(3) Statement of Material Facts
- "SB Noninfringement Add'l Facts"—Plaintiffs' Local Rule 56.1(b)(3) Statement of Additional Facts that Require Denial of TorPharm's Summary Judgment Motion for Noninfringement
- "TP Add'l Facts Resp."—TorPharm's Response to Plaintiff's Local Rule 56.1(b)(3) Statement of Additional Facts That Require Denial of TorPharm's Summary Judgment Motion for Noninfringement

"Paroxetine . . . (free base or any salt)" throughout the world save in specified Scandinavian countries. (TP Exh. 20.) Pursuant to the license agreement, Ferrosan provided Beecham with information on the chemical structure of paroxetine free base and paroxetine hydrochloride, as well as its method for synthesis of paroxetine hydrochloride and analytical test results. (SB Resp. ¶¶ 40-42.)

In the early 1980s, using information obtained from Ferrosan under the license agreement, chemists employed by Plaintiffs ("SmithKline") and located at a pilot plant in Harlow, U.K. worked to improve the process for the manufacture of paroxetine and paroxetine hydrochloride. (SB Resp. ¶ 39-42.) Between 1982 and 1985, the Harlow plant chemists made over 30 batches of paroxetine hydrochloride. (SP Resp. ¶ 41.)

On May 29, 1985, SmithKline scientist Alan Curzons issued a memorandum entitled "Paroxetine Polymorphism." In the memorandum Curzon stated that paroxetine "ha[d] been shown to exist in two discreet [sic] crystalline polymorphic FORMS," a stable, nonhygroscopic hemihydrate and a hygroscopic anhydrate. Curzon further opined that the discovery of the hemihydrate "may offer patent opportunities." The parties dispute whether it was SmithKline scientists who discovered or "invented" the hemihydrate form of paroxetine or whether the hemihydrate was previously conceived by Ferrosan and communicated to SmithKline under the license agreement. They also disagree as to whether and to what extent SmithKline knew during this period that paroxetine in any form would work as an antidepressant.

On October 25, 1985, Plaintiff Beecham Group p.l.c. ("Beecham"), a British corporation, filed a patent application with GB Application Serial Number 8526407 in the British Patent Office ("GB 8526407"). GB 8526407 "relate[d] to crystalline paroxetine hydrochloride, its preparation and its use as a therapeutic agent." (TP Exh. 48, p. 1.) In it, Beecham

specified that the subject invention provided both the hemihydrate and anhydrate forms of crystalline paroxetine hydrochloride, as well as mixtures that contained a major proportion of either form. (*Id.*, p. 3.)

A year later, on October 23, 1986, Beecham filed a patent application in the U.S. Patent and Trademark Office. (TP ¶ 3.) The application included six claims:

1. Crystalline paroxetine hydrochloride hemihydrate.
2. Crystalline paroxetine hydrochloride hemihydrate in substantially pure form.
3. Crystalline paroxetine hydrochloride hemihydrate, having substantially the same X-ray diffractogram as set out in FIG. 1, substantially the same IR spectrum, in a Nujol mull, as set out in FIG. 2, and substantially the same DSC profile as set out in FIG. 3.
4. A process for the preparation of crystalline paroxetine hydrochloride hemihydrate, which process comprises forming a solution of paroxetine hydrochloride and crystallizing said hemihydrate from solution by precipitation or recrystallization.
5. An anti-depressant pharmaceutical composition comprising an effective anti-depressant amount of crystalline paroxetine hydrochloride hemihydrate and a pharmaceutically acceptable carrier.
6. A method of treatment of depression in mammals, which method comprises administering an effective amount of crystalline paroxetine hydrochloride hemihydrate.

The application eventually issued on January 26, 1988, as United States Patent 4,721,723 ("the '723 patent"), the patent in suit. (*Id.*) The '723 patent, entitled "Antidepressant Crys-

talline Paroxetine Hydrochloride Hemihydrate,"[2] relates to an invention that, according to the Abstract, "provides crystalline paroxetine hydrochloride hemihydrate, processes for its preparation, compositions containing the same and its therapeutic use as an anti-depressant." (*Id.*)

On November 1, 1995, Beecham assigned the '723 patent, which is due to expire on December 29, 2006, to Plaintiff SmithKline Beecham Corporation ("SmithKline Beecham"). (SB Resp. ¶ 143.) SmithKline Beecham is a Pennsylvania corporation engaged in the business of research, development, manufacture, and sale of pharmaceutical products throughout the world. Pursuant to the '723 patent, SmithKline markets a paroxetine hemihydrate-based product in the United States under the trademark Paxil®. (SB Public Use Exh. 1 ¶ 3.) Paxil is indicated for use in the treatment of depression, obsessive compulsive disorder, and panic disorder. (*Id.*) According to SmithKline, Paxil is one of the most widely prescribed prescription drugs in the United States. (*Id.*)

In or about May 1998, Defendant TorPharm, Inc. ("TorPharm"), a Canadian corporation, through its United States agent Defendant Apotex Corp. ("Apotex"), filed an Abbreviated New Drug Application ("ANDA") with the Food and Drug Administration for "Paroxetine HCl Tablets." The application contained a "Paragraph IV" certification stating that, to the best of TorPharm's knowledge, the '723 patent would not be infringed by the manufacture, use or sale of the proposed paroxetine HCl Tablets. *See* 21 U.S.C. § 355(j)(2)(A)(vii)(IV). On or about May 12, 1998, TorPharm sent SmithKline a 21 U.S.C. § 355(j)(2)(B) Notice of Certification informing it of the filing of the ANDA. The

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[2] This compound is characterized by a molecular structure in which two paroxetine hydrochloride molecules are bound to one water molecule in each of the repeating internal unit cells of the crystal.

letter offered the following factual and legal basis for TorPharm's assertion that its proposed product would not infringe the '723 patent:

> TorPharm's Paroxetine HCl does not fall within the scope of any of the claims of United States Patent No. 4,721,723 (the '723 patent). All of the claims of the '723 patent are directed to a crystalline paroxetine hydrochloride hemihydrate. TorPharm's Paroxetine HCl is anhydrous.

On June 26, 1998, SmithKline timely filed this patent infringement action pursuant to 35 U.S.C. § 271(e), which makes it an act of infringement to file an ANDA for a drug claimed in a patent. TorPharm answered the complaint and asserted four affirmative defenses, including the invalidity of the patent under 35 U.S.C. §§ 101, 102, 103, and/or 112 and estoppel by reason of statements and representations made to the United States Patent Office to induce the grant of the '723 patent.

In the matter at hand, four of the motions address the validity of the '723 patent. SmithKline asserts that the patent is not invalidated by 35 U.S.C. § 102(f) and (g) and that the hemihydrate was not in public use for more than a year before the patent issued, which would place the substance in the public domain and render it unpatentable. TorPharm has filed a cross-motion on the public use issue and seeks to have the patent invalidated on the grounds that its language is fatally indefinite. Finally, if we deem the patent valid, TorPharm seeks summary judgment that their proposed drug will not infringe the '723 patent.

LEGAL STANDARD

Summary judgment is appropriate when the record, viewed in the light most favorable to the nonmoving party, reveals that there is no genuine issue as to any material fact and that the moving party is entitled to judgment as a matter of law.

Fed. R. Civ. P. 56(c). The moving party bears the initial burden of showing that no genuine issue of material fact exists. *Celotex Corp. v. Catrett*, 477 U.S. 312, 325, 106 S. Ct. 2548 (1986). The burden then shifts to the nonmoving party to show through specific evidence that a triable issue of fact remains on issues on which the nonmovant bears the burden of proof at trial. *Id.* The nonmovant may not rest upon mere allegations in the pleadings or upon conclusory statements in affidavits; it must go beyond the pleadings and support its contentions with proper documentary evidence. *Id.*

The plain language of Rule 56(c) mandates the entry of summary judgment against a party who fails to establish the existence of an element essential to that party's case, and on which that party will bear the burden of proof at trial. "In such a situation there can be 'no genuine issue as to any material fact,' since a complete failure of proof concerning an essential element of the nonmoving party's case necessarily renders all other facts immaterial." *Celotex*, 477 U.S. at 323.

A patent is presumed to be valid, and the burden of demonstrating the invalidity of a patent is on the party asserting the invalidity. 35 U.S.C. § 282. This burden does not shift to the patent holder at any point during the litigation. *T.P. Labs., Inc. v. Professional Positioners, Inc.*, 724 F.2d 965, 971 (Fed. Cir. 1984). It is with these principles in mind that we turn to the merits of the motions before us.

DISCUSSION

I. Prior Conception or Anticipation

In their second amended answer to the complaint, TorPharm raises four affirmative defenses. The first states that the '723 patent is invalid because it fails to comply with "one or more of the provisions of 35 U.S.C. §§ 101, 102, 103 and/or 112." Despite this sweeping statement, which could implicate any combination of no fewer than 10 statutory subsections, the

parties restricted their briefs on this issue to discussion of only § 102(f) and (g). As we are not inclined to engage in an exercise tantamount to statutory roulette, we similarly limit our treatment to those two subsections.

To eliminate the defense, SmithKline must show that the hemihydrate was not invented prior to Alan Curzons' initial description of it in the 1985 memorandum and that it was not anticipated by Ferrosan's earlier activities with the amorphous anhydrate. TorPharm insists that Ferrosan, not Alan Curzons, invented the hemihydrate and that their invention happened before Curzons' purported isolation of the compound in 1985. Sections 102(f) and (g) state that "[a] person shall be entitled to a patent unless . . . he did not himself invent the subject matter sought to be patented, or before the applicant's invention thereof the invention was made in this country by another who had not abandoned, suppressed, or concealed it. . . ." To obtain summary judgment on the issue of anticipation, therefore, SmithKline must do one of two things. Either they must show that the hemihydrate did not exist until Curzons first identified it, or they must show that even if Ferrosan did actually make the hemihydrate before 1985, they did not contemporaneously appreciate that they had done so or communicate their knowledge of the existence of the substance to SmithKline. *See Mycogen Plant Science v. Monsanto Co.*, 243 F.3d 1316, 1335-36 (Fed. Cir. 2001).

Whether a patent is invalid because of prior conception is a question of law. *Fiers v. Revel*, 984 F.2d 1164, 1168 (Fed. Cir. 1993). SmithKline, as the holder of the '723 patent, already holds a position of advantage because issued patents are presumed valid. 35 U.S.C. § 282; *Speedco, Inc., v. Estes*, 853 F.2d 909, 913 (Fed. Cir. 1988). The presumption of validity for an issued patent includes a presumption that the original inventor is named. *Maxwell v. KMart Corp.*, 880 F. Supp. 1323, 1331 (D. Minn. 1995). TorPharm asserts that because Curzons first identified the hemihydrate in a batch

made according to methods Ferrosan had provided to SmithKline, Ferrosan's methods represented a reduction to practice that renders it the true inventor of the hemihydrate. Even assuming *arguendo* that Ferrosan's method invariably resulted in the production of hemihydrate, TorPharm has given us nothing to indicate that Ferrosan appreciated that it had produced the compound or that it communicated that knowledge to SmithKline. Both of these elements are necessary before a patent can be invalidated by prior conception; "an accidental, unappreciated reduction to practice" will not suffice. *Mycogen*, 243 F.3d at 1336.

TorPharm points to another passage in *Mycogen*, which states that a valid prior conception need not recite each limitation of the claim *in haec verba*. 243 F.3d at 1336. We do not quarrel with the accuracy of that statement of law, but *Mycogen* does not stand for the proposition that the language of the claims is irrelevant, particularly under circumstances such as this case. The very crux of the dispute is the difference between hemihydrate and anhydrate. Ferrosan's scientists not only did not call the substance hemihydrate, they never recognized it to be different from the anhydrous material that was the subject of the '196 patent, assuming that they did actually produce the hemihydrate before Curzons' identification. Without such recognition, Ferrosan cannot be said to have "invented" the hemihydrate, and Curzons was the first to identify the substance and is thus correctly deemed its inventor.

A party seeking to invalidate a patent under § 102 is not restricted to showing only prior invention. An invention is just as unpatentable if it is anticipated by prior art. Anticipation of an invention occurs when a single prior art reference or prior reduction to practice discloses each and every element of a claimed invention. *Richardson v. Suzuki Motor Co.*, 868 F.2d 1226, 1236 (Fed. Cir. 1989); *Akzo N.V. v. U.S. Int'l Trade Comm'n*, 808 F.2d 1471, 1479 (Fed. Cir. 1986),

Transco Products, Inc., v. Performance Contracting, Inc., 792 F.Supp. 594, 598 (N.D. Ill. 1992). If even one element is excluded from the prior art reference, the party seeking to invalidate the patent will not be able to show anticipation. *Atlas Powder Co. v. E.I. du Pont De Nemours & Co.*, 750 F.2d 1569, 1574 (Fed. Cir. 1984).

Although this alternative basis for invalidity is theoretically available to TorPharm, the same defects in their prior invention argument prevent its actual application to this case. Ferrosan, even assuming that they did in fact produce hemihydrate, never realized that they had done so. They could not communicate to SmithKline something that they did not know, and any prior art reference to which TorPharm could point would be lacking the single most important element of the '723 patent: the hemihydrate element. We therefore conclude that the hemihydrate was neither anticipated by Ferrosan's activities nor did Ferrosan conceive of the substance prior to Curzons' initial identification.

II. Public Use

Thirty-five U.S.C. § 102(b) sets forth a number of statutory bars to the patentability of an invention. In pertinent part, the section provides that "a person shall be entitled to a patent unless— . . . (b) the invention was . . . in public use . . . in this country, more than one year prior to the date of the application for patent in the United States." Because SmithKline filed its application for the '723 patent on October 23, 1986, the "critical date" for purposes of the § 102(b) public use bar in this case is October 23, 1985; SmithKline began testing the efficacy of the hemihydrate in clinical trials before this date, on May 3, 1985. (TP Public Use Resp. ¶ 36.) Both parties have moved for summary judgment on the issue of whether these five months of trials constitute an invalidating "public use" of the invention under § 102(b).

A. Experimental Nature of the Trials

The U.S. trials were conducted according to detailed clinical protocols prepared by SmithKline and approved by the FDA. In each trial, a doctor-investigator administered either paroxetine HCl hemihydrate tablets or a placebo to patients selected according to criteria set forth in the protocols. Five of the seven clinical trials involving the hemihydrate were "double blinded" in that neither the investigator nor the patient was aware whether the drug administered was the paroxetine or the placebo. (TP Public Use Resp. ¶ 41-42.) In none of the trials was the doctor or patient informed that it was hemihydrate, rather than some other polymorphic form of the compound, that was being tested. (TP Public Use Resp. ¶ 70.) Both were, however aware that the hemihydrate was being administered to some patients as part of the study.

SmithKline controlled the trials in a variety of ways, including establishing the double blind in certain trials and monitoring investigators to ensure that they were following the clinical protocols SmithKline had established. (SB ¶ 60). None of the named inventors of the '723 patent exerted any direct control over or placed limitations on how patients and doctors used the hemihydrate sent to the United States before the critical date. (SB Resp. ¶¶ 371, 373.) Nor did they participate in, supervise, or review the results of the U.S. clinical trials. (SB Resp. ¶ 374.) It was SmithKline, their employer and assignee of the '723 patent, who provided such control and supervision.

The results of the U.S. clinical trials were not included in the application for the '723 patent. (TP Exh. 3.) Indeed, they could not be; none of the double blind studies involving the hemihydrate was completed until December 29, 1986, two months after the patent application was filed. (SB Public Use ¶ 47.) It was not until after this date that SmithKline could dissolve the double blind and begin to analyze the results of

the clinical trials with respect to the efficacy of the hemihydrate in treating depression in humans. (*Id.*)

SmithKline argues that the above-described clinical trials constitute an experimental use of the hemihydrate, not a "public use" within the meaning of 35 U.S.C. § 102(b). Courts have long recognized the principle that "an inventor who seeks to perfect his discovery may conduct extensive testing without losing his right to obtain a patent for his invention—even if such testing occurs in the public eye." *Pfaff v. Wells Elec., Inc.*, 525 U.S. 55, 64 (1999). The reasons for the rule are straightforward:

> It is sometimes said that an inventor acquires an undue advantage over the public by delaying to take out a patent, inasmuch as he thereby preserves the monopoly to himself for a longer period than is allowed by the policy of the law; but this cannot be said with justice when the delay is occasioned by a *bona fide* effort to bring his invention to perfection, or to ascertain whether it will answer the purpose intended. His monopoly only continues for the allotted period, in any event; and it is the interest of the public, as well as himself, that the invention should be perfect and properly tested, before a patent is granted for it." *Pfaff*, 525 U.S. at 64-65 (quoting *Elizabeth v. American Nicholson Pavement Co.*, 97 U.S. 126, 137 (1877)).

In accordance with the goals underlying the experimental use doctrine and the strong public interest in gaining rapid access to useful inventions, courts have limited the types of experimentation that trigger application of the exception. Specifically, the testing must have as its aim "to allow *the inventor* to refine his invention or to assess its value relative to the time and expense of prosecuting a patent application." *In re Hamilton*, 882 F.2d at 1581 (emphasis in original). The experimentation cannot be for the purpose of market testing, *see Smith v. Davis Mfg. Co. v. Mellon*, 58 F. 705, 707 (1893)

(calling market testing "a trader's, not an inventor's, experiment"), commercial profit, *see Smith v. Griggs Mfg. Co. v. Sprague*, 123 U.S. 249 (1887), or testing for suitability for a customer's unclaimed needs, *see, e.g., Cordant Technology, Inc. v. Alliant Techsystems, Inc.*, 45 F. Supp. 2d 398, 406 (D. Del. 1999). Nor can it aim to satisfy regulatory testing requirements unrelated to the claimed features of the patented invention. *Pennwalt Corp. v. Akzona, Inc.*, 740 F.2d 1573, 1580 (Fed. Cir. 1984) (imposing § 102(b) bar where patentee's testing under Environmental Protection Agency experimental use permit had goal of establishing environmental safety, not effectiveness, of patented pesticide).

Ordinarily, courts have required the testing to be carried out by the inventor or someone under his control or surveillance. Although inventor control is not invariably a threshold requirement for application of the experimental use doctrine, it is an "important" factor, *see In re Hamilton*, 882 F.2d 1576, 1581 (Fed. Cir. 1989), and courts have not hesitated to find an invalidating public use where an inventor failed to exert sufficient control over the alleged experimentation. *See, e.g., Egbert v. Lippmann*, 104 U.S. 333 (1881); *Lough v. Brunswick Corp.*, 86 F.3d 1113 (1996); *In re Hamilton*, 882 F.2d 1576 (Fed. Cir. 1989); *Magnetics, Inc. v. Arnold Eng'r Co.*, 438 F.2d 72, 74 (7th Cir. 1971). *Cf. Monon Corp. v. Stoughton Trailers, Inc.*, 239 F.3d 1253 (Fed. Cir. 2001) (vacating finding of public use where district court ignored evidence that inventor actively sought feedback on experiments). The Federal Circuit has explained that the "factor of control is critically important, because, if the inventor has no control over the alleged experiments, he is not experimenting. If he does not inquire about the testing or receive reports concerning the results, similarly, he is not experimenting." *Lough*, 86 F.3d at 1120.

In this case, none of the named inventors planned, supervised, or exerted control over the clinical trials, inquired

about the testing, or received reports concerning the results. TorPharm argues that this lack of participation negates the suggestion that the inventors were using the trials to perfect their invention or to determine whether it would work for its intended purpose and renders the trials a public use within the meaning of § 102(b). SmithKline counters that its own supervision and control of the clinical trials was sufficient to demonstrate that they represented an experimental rather than public use of paroxetine HCl hemihydrate.

No published case has directly addressed the question of whether control of the alleged experimentation by the inventor's employer and assignee of the patent would, in the face of an utter lack of participation by the named inventor, satisfy the inventor control requirement of the experimental use doctrine. Several cases have, however, used the term "patentee" rather than "inventor" when discussing the control requirement, and in such cases courts tend to be concerned with the unrestricted testing of an invention by *third parties* unconnected to the inventor or the patent process. *See, e.g., Baxter International, Inc. v. COBE Labs, Inc.*, 88 F.3d 1054, 1060 (Fed. Cir. 1996); *Petrolite Corp. v. Baker Hughes, Inc.*, 96 F.3d 1423, 1427-28 (Fed. Cir. 1996). For example in *In re Hamilton*, cited by TorPharm, the Federal Circuit commented, "What is remarkable about the tale of experimental use which has been placed before us in this case is the lack of involvement of either the inventor, James Hamilton, *or his employer and assignee*, Western Printing Machinery." 882 F.2d at 1581. These cases suggest that, in appropriate circumstances, the employer/assignee may control the experimentation process in lieu of the inventor.

This reading of the control requirement is consistent with the goals underlying the experimental use doctrine. It is difficult to imagine how unguided testing by a third party without feedback to the parties seeking the patent might play a role in assisting the patent seekers to refine their invention

or demonstrate its efficacy. Where the testing is performed at the behest of a corporation that has invested resources in the development of the invention and that stands to benefit financially from its patenting, on the other hand, the connection is evident. Here, the inventors named in the '723 patent were employed by SmithKline under contracts that transferred to SmithKline all rights to any inventions made during their employment. (Exhs. 1-2 to Pls.' Mem. Opp. TorPharm's Mtn. for Summ. Jdgmt. of Invalidity Based on 35 U.S.C. § 102(b).) It was SmithKline who applied for the '723 patent and to SmithKline that the patent was assigned upon issuance. We conclude that in light of this relationship between SmithKline and the inventors and the rationale behind the experimental use doctrine, the absence of any direct participation by the named inventors in the clinical trials does not itself render the '723 patent invalid.

We also conclude that the control SmithKline actually exercised over the trials was sufficient to demonstrate that the trials were in the nature of experimentation rather than mere commercial use. SmithKline drafted detailed clinical protocols that set forth the manner in which the trials were to be conducted. The protocols instructed investigators on *inter alia* the criteria for selecting patients, the appropriate dosing schedule, and the timing of investigator-patient visits, and they set forth rules regarding the confidentiality of study results. (SB Public Use Exhs. 20-22.) SmithKline met with the investigators to discuss their participation in the hemihydrate trials and had each investigator sign an "Investigator Agreement" stating that the trials would be conducted in accordance with the protocols. (SB Public Use Exhs. 23-24.) Finally, SmithKline employees performed some site visits to ensure that the protocols were being followed. (*See, eg.*, SB Public Use Exhs. 37 at 29 and 38 at 87:14-21.) These controls were significant and strongly indicate the experimental nature of the clinical trials.

TorPharm argues that SmithKline's confidentiality procedures were insufficient to justify invocation of the experimental use doctrine. Confidentiality of test results is indeed one element of the experimental use analysis. *See Baxter International Inc. v. COBE Labs., Inc.*, 88 F.3d 1054, 1060 (Fed. Cir. 1996). However, total secrecy is not required. *See T.P. Labs., Inc. v. Professional Positioners, Inc.*, 724 F.2d 965, 971-72 (Fed. Cir. 1984) (failure of dentist-inventor to obtain confidentiality agreements from subject-patients not indicative of absence of inventor control). It is merely one of several factors. The other factors, including the brief period of time of the precritical date testing and the fact that SmithKline received no payment for the trials, weigh in favor of a finding of experimental use. *See Baxter*, 88 F.3d at 1060. This does not end our inquiry, however, as TorPharm has argued that the period during which SmithKline could experiment with the hemihydrate ended before the critical date because the invention was already "reduced to practice."

B. Reduction to Practice

Numerous Federal Circuit cases have recited the rule that experimental use necessarily ends when the invention at issue is "reduced to practice." *See, e.g., RCA Corp. v. Data Gen. Corp.*, 887 F.2d 1056, 106 (Fed. Cir. 1989); *Atlantic Thermoplastics Co. v. Faytex Corp.*, 5 F.3d 1477, 1480 (Fed. Cir. 1993); *Baxter*, 88 F.3d at 1060-1061. Reduction to practice of a pharmaceutical compound means that the inventor "'actually prepared the composition and knew it would work.'" *Estee Lauder, Inc. v. L'Oreal S.A.*, 129 F.3d 588, 592 (Fed. Cir. 1998) (quoting *Hahn v. Wong*, 892 F.2d 1028, 1032 (Fed. Cir. 1989)). As discussed above, precritical date experimental use of an invention evades the § 102(b) public use bar only when the experimentation represents a bona fide effort to perfect the invention or to ascertain whether it will answer its intended purpose. Because an invention that has been reduced to practice is by definition shown to work for its

intended purpose, reduction to practice necessarily ends any effort to perfect the invention and ascertain its effectiveness. It thus concludes the period during which use may be considered experimental for purposes of the § 102(b) bar.

SmithKline argues that the Supreme Court's decision in *Pfaff v. Wells Electronics, Inc.*, 525 U.S. 55, 119 S. Ct. 304 (1998), overturned this rule. In *Pfaff*, the Court reversed a Federal Circuit decision that had held that an invention must be reduced to practice for the on-sale bar of 35 U.S.C. § 102(b) to apply. In so holding, the Court established a two-part test for application of the on-sale bar: (1) the product must have been the subject of a "commercial offer for sale," as opposed to an experimental use; and (2) the product must have been "ready for patenting" at the time the offer was made. *Id.* at 67-68. Although proof of reduction to practice is one method of satisfying the ready-for-patenting prong of the test, the Court held, it is not the only means. *Id.* Rather, an invention that is sufficiently outlined or described to enable persons skilled in the art to practice it may be ready for patenting even if it is not yet reduced to practice. *Id.*

Pfaff thus stands primarily for the proposition that "just because reduction to practice is sufficient evidence of completion [of an invention] does not mean that proof of reduction to practice is necessary in every case." 525 U.S. at 66. The decision does not address the related question of whether a reduction to practice is relevant only to the question of whether the invention is ready for patenting or whether it may also bear on the question of whether the nonprivate use of the invention was public or experimental. The only post-*Pfaff* Federal Circuit case to mention the issue followed the latter approach, but only in nonbinding dicta. *See Zacharin v. United States*, 213 F.3d 1366, 1368 (Fed. Cir. 2001) ("The trial court rejected [the experimental use] argument because the parties stipulated that the invention had been reduced to practice before the [] contract was awarded, and once an

invention has been reduced to practice, it can no longer meet the experimental use exception. *See RCA Corp. v. Data Gen. Corp.*, 887 F.2d 1056, 1061, 12 USPQ2d 1449, 1453 (Fed. Cir. 1989).")

As discussed above, the reduction to practice rule essentially mirrors the unchallenged requirement that any qualifying experimental use be aimed at perfecting the invention or testing its effectiveness. It is the opinion of this court that the reduction to practice rule set forth in *RCA Corp. v. Data Gen. Corp.* 887 F.2d 1056, 1061 (Fed. Cir. 1989) continues to apply after *Pfaff*. We must therefore proceed to determine whether the invention covered by the '723 patent was reduced to practice prior to the critical date of October 23, 1985. The analysis entails legal questions based on underlying facts. *See Estee Lauder, Inc. v. L'Oreal S.A.*, 129 F.3d 588, 592 (Fed. Cir. 1998). To the extent that such facts are undisputed, the issue may be ripe for summary judgment.

"To prove actual reduction to practice, an inventor must establish that he 'actually prepared the composition and knew it would work.'" *Estee Lauder, Inc. v. L'Oreal S.A.*, 129 F.3d 588, 592 (Fed. Cir. 1998) (quoting *Hahn v. Wong*, 892 F.2d 1028, 1032 (Fed. Cir. 1989)). The parties agree that SmithKline had actually prepared the hemihydrate prior to the critical date of October 23, 1985; the dispute is over whether SmithKline knew the hemihydrate was suitable for its intended purpose—treating depression in humans—before that date. SmithKline claims that its earlier laboratory and clinical tests were inconclusive and that the controlled clinical trials in the U.S. were required for it to establish the efficacy of the drug. TorPharm contends that SmithKline knew paroxetine HCl hemihydrate was effective to treat depression before the critical date, and that the U.S. clinical trials were carried out for the sole purpose of meeting stringent FDA regulatory requirements regarding proof of the safety and efficacy of drugs to be sold on the U.S. market.

It is clear from the evidence presented by both parties that SmithKline had, prior to the critical date, some indication that paroxetine HCl hemihydrate was likely to work as an antidepressant in humans. Indeed, to obtain the '196 and '723 patents, Ferrosan and SmithKline represented to the patent office that paroxetine and paroxetine HCl hemihydrate, respectively, were useful as antidepressants. *See* '196 patent, TP Exh. 4, col. 8, ln. 27; '723 patent, TP Exh. 3, claims 5-6). In the application for the '196 patent, Ferrosan supported its utility claims with in vitro tests performed on rat brains that showed that the serotonin uptake inhibitory activity of paroxetine maleate compared favorably with the inhibitory activity of then-common antidepressant drugs like Imipramine and Amitriptyline. (TP Exh. 4, Col. 8, lns. 30-44.) It also determined that paroxetine maleate had fewer cardiovascular side effects in animals than did drugs in the Imipramine family. (*Id.*, col. 8, lns. 44-54.) When SmithKline applied for the '723 patent in October 1985, it provided no additional scientific evidence of the effectiveness of paroxetine in treating depression, relying instead on data recited in the '196 patent. (TP Exh. 3, col. 1.) According to TorPharm, this is because the active moiety in both inventions—paroxetine—is the same; if paroxetine is effective at treating depression when used in the form of a maleate salt, as in the '196 patent, it will be effective when used in any crystalline form, including hemihydrate.

TorPharm also cites animal and human efficacy studies performed by Ferrosan and SmithKline in Europe in the early 1980s, before Curzons reportedly discovered the hemihydrate. SmithKline denies that these studies demonstrated that paroxetine worked as an antidepressant in humans. It cites design flaws in the studies including the low number and imprecise selection of patients and the absence of the double blind it claims is essential in establishing the efficacy of a drug designed to treat a psychological, rather than physiological, condition. (*See, e.g.*, Decl. of Jeffrey S. Simon, SB

Public Use Exh. 14, ¶ 7.) In addition, SmithKline points out that its early clinical trials involving humans and animals utilize anhydrous paroxetine, rather than the hemihydrate covered in the '723 patent. SmithKline disputes TorPharm's suggestion that proof of the effectiveness of the anhydrate sufficed as proof that the hemihydrate, too, would work to treat depression. According to SmithKline's experts, "'only clinical trials would be sufficient to demonstrate the bio-availability and efficacy of paroxetine HCl hemihydrate as an antidepressant.'" (Decl. of Dr. Stephen R. Byrn, attached as Exh. 5 to Pls.' Mem. Opp. TorPharm's Mtn. for Summ. Jdgmt. Based on 35 U.S.C. § 102(b), ¶¶ 26-28.) Such trials, SmithKline argues, were not begun with the hemihydrate until May 1985, and the results were not in until after the '723 patent application was filed. TorPharm would have us hold that controlled clinical trials involving human subjects are, as a matter of law, never required for a pharmaceutical manufacturer to demonstrate that a new drug is effective for its intended purpose. The Federal Circuit has held that FDA-mandated testing procedures are not necessary before a pharmaceutical company may *seek a patent* on a new drug. *See In re Brana*, 51 F.3d 1560, 1568 (Fed. Cir. 1995); *In re Hartop*, 311 F.2d 249, 259-60 (C.C.P.A. 1962). However, as the Supreme Court recently noted in *Pfaff, supra*, "[i]t is well settled that an invention may be patented before it is reduced to practice." The cases cited by TorPharm are therefore not dispositive on the reduction to practice issue.

The Federal Circuit has noted that in determining reduction to practice, courts are "guided by a common sense approach in weighing the sufficiency of the testing." *Scott v. Finney*, 34 F.3d 1058, 1061 (Fed. Cir. 1994). Humans and rats are not wholly dissimilar, but it is well within the realm of common sense that tests showing decreased uptake of a particular substance in rat brains indicates only a possibility of like chemical behavior in the human cerebrum. It is beyond peradventure that the animal studies would not conclusively

prove anything about the effect of such a drug on a complex condition such as human depression and anxiety disorder.

In addition, it is well settled that use in a country other than the United States, without accompanying publication or foreign patent, cannot operate to invalidate an issued American patent. 35 U.S.C. § 102(b) ("[a] person shall be entitled to a patent unless . . . the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale *in this country*, more than a year prior to the date of the application for patent in the United States) (emphasis added); *see also, e.g., Elizabeth*, 97 U.S. at 130; *Milwaukee v. Activated Sludge, Inc.*, 69 F.2d 577, 589 (7th Cir. 1934); *Badowski v. United States*, 164 F. Supp. 252, 255 (Ct. Cl. 1958). None of the Ferrosan human or animal trials were conducted within the United States. The only foreign publication or patent, the British patent application, was filed less than one year before the American application; it cannot qualify as an invalidating event under § 102(b). Accordingly, SmithKline is entitled to summary judgment that the '723 patent is not invalidated by prior public use.

III. Indefiniteness

TorPharm has moved for summary judgment of invalidity of the '723 patent on the ground that the patent is fatally indefinite within the meaning of 35 U.S.C. § 112. The second paragraph of that section provides that the specification in a patent application "shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention." TorPharm argues that to the extent that the claims in the '723 patent comply with this section, they cannot support a claim of infringement. To the extent that the claims are construed more broadly to encompass the product identified in TorPharm's ANDA, TorPharm argues, they fail to comply with the particularity requirements of section 112. We address the question of noninfringement in Section IV, *infra*,

but because analysis of both indefiniteness and noninfringement hinge on the meaning of the claim language, we begin with a construction of claim 1. *Exxon Research and Engineering Co. v. United States*, 265 F.3d 1371, 1375 (Fed. Cir. 2001); *Bayer AG v. Elan Pharmaceutical Res. Co.*, 212 F.3d 1241, 1247 (Fed. Cir. 2000).

A. Scope of the Claims

Although we have not performed a formal *Markman* hearing in this case, in light of the parties' full briefing on the issues before us and the oral presentations they have given, we have sufficient information at our disposal to allow us to construe the meaning and scope of claim 1.

Claim 1 of the '723 patent reads simply "[c]rystalline paroxetine hydrochloride hemihydrate." The parties disagree as to the scope of this seemingly plain language. SmithKline contends that claim 1 covers crystalline paroxetine hydrochloride hemihydrate in any amount or in mixtures with other polymorphic forms of paroxetine hydrochloride. TorPharm argues that the claim covers only those paroxetine compositions that consist of pure hemihydrate. According to TorPharm, a paroxetine composition that is primarily anhydrous but contains small numbers of hemihydrate crystals is not covered by the language of the claim. The distinction is a critical one, as SmithKline claims that the product proposed in TorPharm's ANDA, while primarily anhydrous, contains some number of hemihydrate crystals.

Three sources of information are properly considered in claim construction: first and foremost, the claims themselves, then the specification and prosecution history if the claim language is not clear on its face. *Markman v. Westview Instruments, Inc.*, 52 F.3d 967, 979 (Fed. Cir. 1995), *aff'd* 517 U.S. 370 (quoting *Unique Concepts, Inc. v. Brown*, 939 F.2d 1558, 1561 (Fed. Cir. 1991)); *Gart v. Logitech, Inc.*, 254 F.3d 1334, 1341 (Fed. Cir. 2001). Patents must be read in light of

their specifications, without reading limitations from the description into to a claim. *Scimed Life Systems, Inc. v. Advanced Cardiovascular Systems, Inc.*, 242 F.3d 1337, 1340-42 (Fed. Cir. 2001).

In construing claim 1 of the '723 patent, we begin from the general principle that "terms in the claim are to be given their ordinary and accustomed meaning." *Gart*, 254 F.3d at 1341. Claim 1 consists of the four words "[c]rystalline paroxetine hydrochloride hemihydrate"; it does not specify whether this compound must be present alone or may be found in mixtures with other substances or polymorphic forms. Claim 2 sheds some initial light on the question; it reads "[c]rystalline paroxetine hydrochloride hemihydrate in substantially pure form." Under the doctrine of claim differentiation, we may not read into an independent claim a limitation explicitly set forth in another claim. *See, e.g., Environmental Designs Ltd. v. Union Oil Co. of Calif.*, 713 F.2d 693, 699 (Fed. Cir. 1985). We therefore cannot interpret claim 1 to contain the "substantially pure" limitation.

TorPharm attempts to reconcile claims 1 and 2 by arguing that "substantially pure" in claim 2 means "substantially free of transesterification by-products." They urge that we look to the specification to determine the meaning of claim 2, but this is unnecessary under the circumstances. Claim 2 is not so unclear that there is no means by which its scope can be ascertained from the plain language used. It is well settled that a patentee can be his or her own lexicographer, using terms in a manner inconsistent with their ordinary meanings. Special definitions given to a word not used according to its ordinary meaning must be clearly defined in the specification, but the written description guides the meaning of the claims even if the guidance does not appear in the express format of a definition. *Markman*, 52 F.3d at 980; *Scimed Life Systems*, 242 F.3d at 1344. SmithKline has not chosen to be its own lexicographer in the specification by precisely defining the

term "substantially pure." TorPharm points to the following passage of the specification, arguing that it creates a limitation on claim 2:

> In the above mentioned U.S. Patent No. 4,007,196, for the preparation of paroxetine (Examples 1 and 2), an N-Methyl compound is reacted with phenyl chloroformate and the resultant compound is hydrolysed with potassium hydroxide.
>
> One disadvantage of this process is that the solvent used during the hydrolysis step (methyl cellosolve) leads to the production of unwanted transesterification by-products.
>
> We have now discovered that the purity of the final product can be improved by using a different solvent during the hydrolysis step, such as toluene . . . .
>
> The pure paroxetine free base thus obtained can then be used for the preparation of crystalline paroxetine hydrochloride hemihydrate as set out above. (TP Exh. 3, col. 3, lines 1-18.)

TorPharm is correct in asserting that this passage sets forth a procedure by which unwanted transesterification by-products are minimized. However, it refers only indirectly to the purity of the final product. The elimination of the transesterifcation by-products occurs during the preparation of the paroxetine free base.[3] It does not follow that the only potential impurities that could appear in a substance covered by claim 2 are transesterification by-products. Indeed, claim 2 represents the preferred embodiment of the claimed sub-

---

[3] Paroxetine free base refers to the compound paroxetine in isolation, before the hydrochloride is added to form the paroxetine salt and without the crystalline structure or presence of water that distinguish the material named in claim 1.

stance, which would of necessity contain substances other than the hemihydrate to facilitate biodelivery. At most, the passage cited by TorPharm provides one example of an impurity that is eliminated with the patented invention. It does not explicitly limit the meaning of any terms in claim 2.

Because SmithKline has not provided a customized definition of the phrase "substantially pure," we must "give full effect to the ordinary and accustomed meaning of [the] terms" in claim 2. The ordinary and accustomed meaning of the phrase "in substantially pure form" is "substantially free of any impurities." The term "substantially" could be problematic in that it does not inherently suggest a set range of purity levels. However, the Federal Circuit recently held that the term "substantial," while making the claim language less than ideally precise, leaves those skilled in the art with some indication of its boundaries. *Exxon*, at 1375, 1378. In any event, we need not decide the exact meaning or precision level of this term, because this case does not turn on the language of claim 2. Our only concern is the language of claim 1, which by application of the claim differentiation doctrine cannot be read to contain a limitation of substantial purity, whatever the exact meaning of that term is. In other words, it cannot be read, as TorPharm suggests, to exclude "'mixtures' and any other composition that contains, but is not purely, crystalline paroxetine hydrochloride hemihydrate." (*See* TP Mem. in Supp. of its Mtn. for Summ. Jdgmt. of Noninfringement, p. 27.)

The hemihydrate, at the time it was patented, was a novel material and so deserving of broader protection than a simple improvement of an existing material. *CITE* It does not necessarily follow, however, as SmithKline would have us believe, that claim 1 covers any modicum of the hemihydrate found in any mixture with other substances or polymorphic forms. While two distinct claims cannot ordinarily be read to have the same meaning, the doctrine of claim differentiation

cannot broaden claims beyond the scope that is supported by the specification. *Multiform Desiccants, Inc. v. Medzam Ltd.*, 133 F.3d 1473, 1480 (Fed. Cir. 1998). TorPharm argues along these lines that the specification and prosecution history of the '723 patent impose limits on the invention that exclude from the ambit of claim 1 compositions that are primarily anhydrous but that contain a few incidental crystals of the hemihydrate. We find that the language of claim 1 is sufficiently unclear on this point that consideration of the specification and prosecution history are in fact appropriate. *See Gart*, 254 F.3d at 1341; *see also Glaxo, Inc. v. Novopharm Ltd.*, 110 F.3d 1562, 1566 n.1 (Fed. Cir. 1997) (eschewing disputed issue of whether small amounts of patented material present in mixture with public domain material would infringe patent and if so what amounts would be required).

The specification of the '723 patent does not assign a particular nonordinary meaning to any of the terms in claim 1. It does, however, describe certain properties of the substance, such as melting point and water to paroxetine ratio, and enumerates characteristic indicia of the hemihydrate when subjected to certain testing methods such as infrared spectroscopy and X-ray diffractography. *Cf. Amgen, Inc., v. Hoechst Marion Roussel*, 126 F. Supp. 2d 69, 155 (D. Mass. 2001) (finding that a detailed description will not distinguish a purportedly novel material when the methods of comparison are based on a "standardless standard"). In addition, the specification describes the hemihydrate as being stable and nonhygroscopic (i.e., not readily absorbing water from the air). These properties distinguish the new material from the prior art anhydrate and thus establish its patentability.

The prosecution history of the '723 patent sheds little illumination on the proper construction of claim 1. At no point did the claim examiner challenge the propriety of its language, giving us no amendments by SmithKline to guide our understanding of exactly what they intended to exclude

from claim 1. *See Warner-Jenkinson Co., Inc., v. Hilton Davis Chemical Co.*, 520 U.S. 17, 40-41 (1997); *Genentech, Inc., v. Wellcome Foundation Ltd.*, 29 F.3d 1555, 1562 (Fed. Cir. 1994). TorPharm greatly emphasizes the language of an earlier British patent application that specifically claimed mixtures of the hemihydrate and anhydrate, insisting that the absence of similar language from the '723 patent disclaims mixtures containing hemihydrate. We disagree with their assessment of the significance of the British application. In at least three places the American patent contemplates substances made up of less than 100% hemihydrate: in claim 2; in the abstract, which refers to compositions containing hemihydrate; and in example 8 of the specification. We will therefore not read the limitations of the British application over the language of the issued American patent.

As recently explained by the Federal Circuit, the proper standard for assessing the definiteness of claim language focuses on one skilled in the art. If such a person "would understand the bounds of the claim when read in light of the specification, then the claim satisfies section 112 paragraph 2." *Exxon*, at 1375. In other words, the claims at issue need not be perfectly precise but must allow potential competitors some guidance in a prospective determination of whether they are infringing an existing patent. *Exxon* at 1375. Claims that are difficult to construe are not automatically indefinite; rather a claim must be "insolubly ambiguous" with no proper narrowing construction before it will be deemed invalid for indefiniteness. *Exxon* at 1375. In addition, issued patents are presumed valid to "protect the inventive contribution of patentees, even when the drafting of their patents has been less than ideal." *Exxon*, at 1375. This statutory presumption requires courts to resolve close questions of indefiniteness in favor of the patent holder. *Exxon* at 1380.

In light of the holding in *Exxon*, for TorPharm to prevail on this motion, they must prove as a matter of law that one

skilled in the art would not understand the bounds of the claim when it is read in light of the specification. This they have not done. The characteristics of the hemihydrate are sufficiently laid out and different enough from those of the anhydrate that the claim is not fatally indefinite. The language satisfies the standard cited in *Exxon*, and it is not invalid for indefiniteness.

IV. Noninfringement

Having concluded that the '723 patent is valid, we must move on to the issue of infringement of the '723 patent. TorPharm moves for summary judgment of noninfringement, alleging that the product identified in its ANDA is an anhydrous form of crystalline paroxetine hydrochloride and thus that it does not fall within the scope of the claims of the '723 patent. SmithKline does not contend that paroxetine hydrochloride anhydrate would infringe the '723 patent. Rather, its complaint centers on a contention that the commercial drug product TorPharm will produce if its ANDA is approved by the FDA will contain crystalline paroxetine hydrochloride hemihydrate and thereby infringe claim 1 of the '723 patent. SmithKline has not moved for summary judgment of infringement, so we consider only whether TorPharm has successfully borne the burden of showing that no genuine issue of material fact exists and that as a matter of law their proposed product will not infringe SmithKline's patent.

A. Testing Methods

As stated earlier, the specification of the patent-in-suit states several distinguishing properties of the claimed substance. Of course, the enumeration of these properties means little unless their presence in an allegedly infringing substance can be accurately detected and measured. The testing methods employed are therefore an indispensable part of the infringement analysis in this case.

TorPharm argues that the presence of hemihydrate in its proposed product can be measured only using the testing methods to which the patent specifically refers or at least methods that were available at the time the patent issued. To allow SmithKline to use other, newer methods would undermine the notice function of patents and would cause a patent to mean different things at different times depending on the state of the art in measurement technology. *See Abbott Laboratories v. Alra Laboratories, Inc.*, 1997 WL 667796 (N.D. Ill. Oct. 24, 1997). They insist that the methods discussed in the specification do not show that their product exhibits any of the properties that SmithKline listed as identifying the hemihydrate and thus their proposed drug does not infringe claim 1. They take issue with the testing methods that SmithKline used to determine that their product contained hemihydrate for the purposes of this litigation. They contend that these methods are not the ones cited in the specification and their results are therefore impermissible. SmithKline counters that the tests used to determine infringement need not be the same ones mentioned within the patent language itself, and they claim that the tests they used to measure TorPharm's drug were available when the '723 patent issued. *American Cyanamid Co. v. U.S. Surgical Corp.*, 833 F. Supp. 92, 130-31 (D. Conn. 1992) ("proof of infringement is not limited to methods in existence on the date of the invention"); *Cosden Oil & Chemical Co. v. American Hoechst Corp.*, 543 F. Supp. 522, 530 (D. Del. 1982) (foreseeing "no advantage and considerable mischief in freezing measurement technology and disregarding new learning which can establish . . . the precise characteristics of the accused substance"). We agree with these authorities and SmithKline that they are not limited to only the tests to which the patent specifically refers for determining infringement.

B. Timing

Although important, the decision regarding which testing methods are permissible is not the end of the inquiry. The

timing of the measurement is also crucial, especially with a substance such as the paroxetine salt, which SmithKline attests will change composition over time and when subjected to everyday temperature and humidity conditions. Given the wide range of possible times for testing, and the correspondingly varying results, the Federal Circuit has ruled that the time at which the composition of a drug proposed in ANDAs is legally significant for infringement purposes is the time of marketing. Any changes in the chemical composition after the product is marketed are simply not relevant to an infringement analysis.

SmithKline makes much of tests it performed simulating the exposure to moisture TorPharm's product would undergo when patients taking the drug repeatedly opened and closed the bottles that contained the drugs. However, because these conditions would occur after the time of marketing, the results of these test are not relevant to our inquiry. TorPharm has supplied us with the levels of purity required of their product both when it ships to them from the supplier of their raw materials, BCI (TP Exhs. 242, 243) and their internal analysis specifications (TP Exhs. 244, 245). However, the numbers in these documents indicate only how much of TorPharm's product is not the crystalline anhydrate, not what substances make up the "contaminants." To decide infringement, we must know whether, and how much, of the impurity is made up by a demonstrable amount of hemihydrate. Based on the parties' submissions, the facts required for us to make such a determination are very much in dispute, and we therefore cannot find as a matter of law that TorPharm's product does not and cannot infringe the '723 patent.

What amount of hemihydrate is necessary to allow detection of these properties is unclear and necessarily involves issues of fact that are not properly resolved on a motion for summary judgment.

CONCLUSION

For the foregoing reasons, we grant Plaintiffs' motions for summary judgment on the issues of the validity of the '723 patent under 35 U.S.C. § 102(b), (f), and (g). We deny Defendant's motions on the issues of invalidity under 35 U.S.C. §§ 102(b) and 112 and noninfringement of the '723 patent.

/s/ Charles P. Kocoras
Charles P. Kocoras
United States District Judge

Dated: December 3, 2001

APPENDIX G

UNITED STATES COURT OF APPEALS
FOR THE FEDERAL CIRCUIT

[Filed Jun 15, 2005]

03-1285, -1313

SMITHKLINE BEECHAM CORPORATION and
BEECHAM GROUP, P.L.C.,
Plaintiffs-Appellants,

v.

APOTEX CORP., APOTEX, INC., and TORPHARM, INC.,
Defendants-Cross Appellants.

ORDER

A petition for rehearing en banc having been filed by the APPELLANTS,* and a response thereto having been invited by the court and filed by the CROSS-APPELLANTS, and the matter having first been referred as a petition for rehearing to the panel that heard the appeal, and thereafter the petition for rehearing en banc and response having been referred to the circuit judges who are in regular active service,

UPON CONSIDERATION THEREOF, it is

ORDERED that the petition for rehearing be, and the same hereby is, DENIED and it is further

ORDERED that the petition for rehearing en banc be, and the same hereby is, DENIED.

The mandate of the court will issue on June 22, 2005.

Circuit Judge LOURIE did not participate in the vote.

---

* The Washington Legal Foundation filed an amicus curiae brief.

FOR THE COURT,

/s/ Jan Horbaly
JAN HORBALY
Clerk

Dated: June 15, 2005

cc: Ford F. Farabow, Jr.
Hugh L. Moore
R. Samp, C. Sipes, C. Siwik
P. Berghoff, R. Hutz, F. Rein

SMITHKLINE BEECHAM V APOTEX, 03-1285, -1313
(DCT - 98-CV-3952)

4

No. 05-489

Supreme Court, U.S.
FILED
NOV 16 2005
OFFICE OF THE CLERK

IN THE

Supreme Court of the United States

SMITHKLINE BEECHAM CORPORATION, *et al.*,

Petitioners,

v.

APOTEX CORPORATION, APOTEX, INC.
and TORPHARM, INC.,

Respondents.

ON PETITION FOR A WRIT OF CERTIORARI TO THE
UNITED STATES COURT OF APPEALS
FOR THE FEDERAL CIRCUIT

BRIEF IN OPPOSITION

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CORPORATE DISCLOSURE STATEMENT

Respondents, Apotex Corp., Apotex, Inc. and Torpharm, Inc. are listed in the caption and are the real parties in interest. Parent corporations are Apotex Pharmaceutical Holdings, Inc. (parent of Torpharm, Inc. and Apotex, Inc.) and Apotex Holdings, Inc. (parent of Apotex Corp.).

No public company holds 10% or more of any of the corporate parties' stock.

TABLE OF CONTENTS

	Page
Corporate Disclosure Statement	i
Table of Contents	ii
Table of Cited Authorities	iv
Statement of the Case	1
Reasons for Denying the Petition	5
I. The Federal Circuit's decision is consistent with long-established law of inherent anticipation and presents no conflict with any decision of this Court.	8
A. It has long been the law that a claim is invalid where its subject matter is inherent in the prior art, regardless of whether that subject matter was appreciated when the application for the patent was filed.	8
B. There is no conflict with any decision of this Court.	11
C. SmithKline's other authority is not on point.	13
II. The Federal Circuit's decision does not discourage innovation.	15

Contents

	Page
III. If the Court grants the writ, then review of other issues will be required.	18
Conclusion	19

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Page

Cases:

Ansonia Brass & Copper Co. v. Electric Supply Co., 144 U.S. 11 (1892) 10

Atlas Powder Co. v. IRECO Inc., 190 F.3d 1342 (Fed. Cir. 1999) 9, 10

Bonito Boats, Inc. v. Thunder Craft Boats, Inc., 489 U.S. 141 (1989) 5

Burr v. Duryee, 68 U.S. 579 (1863) 6

Carnegie Steel Co. v. Cambria Iron Co., 185 U.S. 403 (1902) 11, 12, 13

Continental Can Co. USA, Inc. v. Monsanto Co., 948 F.2d 1264 (Fed. Cir. 1991) 15

Ecolochem, Inc. v. Southern Cal. Edison Co., 863 F. Supp. 1165 (C.D. Cal. 1994), *aff'd in part, rev'd in part on other grounds*, 1996 U.S. App. LEXIS 13330 (Fed. Cir., June 5, 1996), *cert. denied*, 532 U.S. 974 (2001) 12

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Cited Authorities

	Page
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General Electric Co. v. Jewel Incandescent Lamp Co., 326 U.S. 242 (1945)	10
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Granfinanciera, S.A. v. Nordberg, 492 U.S. 33 (1989)	18
In re Bergstrom, 427 F.2d 1394 (C.C.P.A. 1970)	17
In re Buspirone Patent Litigation, 185 F. Supp. 2d 340 (S.D.N.Y. 2002)	17
In re Coordinated Pretrial Proceedings in Antibiotic Antitrust Actions, 498 F. Supp. 28 (E.D. Pa. 1980), *aff'd*, 676 F.2d 51 (3d Cir. 1982)	14
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In re Omeprazole Patent Litigation, 2001 U.S. Dist. LEXIS 7103 (S.D.N.Y. May 31, 2001)	17
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Cited Authorities

	Page
In re Shetty, 566 F.2d 81 (C.C.P.A. 1977)	10
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Silvestri v. Grant, 496 F.2d 593 (C.C.P.A. 1974)	15
Singer Mfg. Co. v. June Mfg. Co., 163 U.S. 169 (1896)	5
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Page

State of North Carolina v. Chas. Pfizer & Co., 384 F. Supp. 265 (E.D.N.C. 1974) 14

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Toro Co. v. Deere & Co., 355 F.3d 1313 (Fed. Cir. 2004) 15

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Statutes:

35 U.S.C. § 101 18

35 U.S.C. § 102 ..... 13, 18

35 U.S.C. § 102(b) 18

35 U.S.C. § 103 18

Other Authorities:

1 DONALD S. CHISUM, CHISUM ON PATENTS § 3.02[1] (2005) 7

ROBERT FABER, LANDIS ON MECHANICS OF PATENT CLAIM DRAFTING § X-2 (5th ed. 2001) 16

STATEMENT OF THE CASE

The '196 and '723 patents.

In 1977, a Danish company named Ferrosan obtained a patent—U.S. Patent No. 4,007,196 (the '196 patent)—on a new class of antidepressant compounds, particularly paroxetine and its salts. App. 2a, 113a. The '196 patent disclosed to the public how to make paroxetine salts, including paroxetine hydrochloride. *Id.* SmithKline later secured from Ferrosan a license to the patent and proceeded to commercialize paroxetine hydrochloride as an antidepressant drug. *Id.*

The '196 patent expired in 1992, and thus the public is free to make everything disclosed in it. *Id.* at 127a.

In 1985, a SmithKline employee noticed that recently made batches of paroxetine hydrochloride had somehow "morphed" from an anhydrate form to what he called a hemihydrate form. *Id.* at 114a. Although SmithKline's request for certiorari in this Court rests on the assumption that this hemihydrate crystalline form, *i.e.*, a different polymorph of paroxetine hydrochloride, was unknown and unknowable at the time (Pet. at 7-8), a SmithKline chemist, Ian Lynch, has admitted that polymorphism—*i.e.*, the tendency of the same chemical compound to exist in a variety of different crystalline forms—was a known phenomenon, and hence it was not unexpected. He explained that "polymorphism of an organic compound should not come as a surprise" and called it a "guilty until proven innocent situation." (Lynch Dep. 236:22 to 237:2, 237:5 to 238:17, 238:20 to 239:19, Tr. at 213:11-13, Pretrial Order at Ex. 43); (DTX 178 at 5).

In any event, SmithKline ultimately obtained a patent—U.S. Patent No. 4,721,723 (the '723 patent), the patent-in-suit here—on this hemihydrate form. The '723 patent expires in December 2006. App. 127a.

The '723 patent has six claims, but SmithKline asserted only claim 1 against Apotex, and thus that is the only claim that the Federal Circuit invalidated. *Id.* (SmithKline is thus wrong to imply, in the Question Presented and in other parts of its petition, that the entire patent was held invalid. (Pet. at i, 3, 8, 10)). Claim 1—the broadest of the claims—reads, simply, "[c]rystalline paroxetine hydrochloride hemihydrate." App. 3a. SmithKline urged, and the Federal Circuit adopted, a construction of claim 1 that extends to the limit of logic to include *any* amount of the hemihydrate, however insignificant—even a single unwanted and undetectable crystal in a batch of prior art anhydrate. *Id.* at 14a.

Apotex's product.

The active ingredient in Apotex's generic drug product is paroxetine hydrochloride anhydrate, *i.e.*, a public-domain form of paroxetine hydrochloride. *Id.* at 3a, 122a. At the infringement trial, however, SmithKline introduced testimony of its retained experts describing a "disappearing polymorph" theory. *Id.* at 120a. According to this theory, as applied to paroxetine hydrochloride, the paroxetine hydrochloride anhydrate that Ferrosan patented is unstable and morphs to some extent into a more stable form, which happens to be the hemihydrate. *Id.* at 126a-27a. SmithKline's experts theorized that the general environment has become "seeded" with crystals of the hemihydrate, and that the production of anhydrate will inevitably, due to the presence of hemihydrate "seeds," result in paroxetine hydrochloride anhydrate contaminated with some unavoidable trace amount of the hemihydrate. *Id.* at 122a-24a.

The district court rejected as fatally flawed SmithKline's efforts to demonstrate, using empirical tests, the presence of hemihydrate in Apotex's product. *Id.* at 144a. Consequently, SmithKline was forced to rely on a circumstantial inference, adopted by the district court and affirmed by the Federal Circuit, that Apotex's manufacture of paroxetine hydrochloride anhydrate inevitably would produce trace quantities of paroxetine hydrochloride hemihydrate through a process of conversion of a small amount of anhydrate to hemihydrate. *Id.* at 14a, 148a. Given the extremely broad "single crystal" construction of claim 1, and the inference, from the novel inevitable-production theory, that Apotex's product must contain at least one such crystal of the hemihydrate, the Federal Circuit determined that Apotex's anhydrate product infringes claim 1 of the '723 patent. *Id.* at 14a. Thus would SmithKline enjoin the public from practicing the prior art of the expired '196 patent.

Federal Circuit holds '723 patent invalid as anticipated by the '196 patent.

But one who lives by the sword also dies by the sword. The same inevitable production of trace or undetectable amounts of the hemihydrate that required a finding of infringement of claim 1 also served to invalidate claim 1, which covers even a single crystal of hemihydrate, for inherent anticipation. That is because a patent is invalid for anticipation if a single prior art reference—here the '196 patent—discloses, expressly or inherently, each and every limitation of the claimed invention. And because "[t]he '196 patent discloses a method of manufacturing PHC anhydrate that naturally results in the production of PHC hemihydrate," the Federal Circuit held that claim 1 of the '723 patent is inherently anticipated by the '196 patent. *Id.* at 19a. Hence,

the Federal Circuit thwarted SmithKline's effort to breathe new life into the '196 patent that expired 13 years ago.

And that is all it did. The Federal Circuit's ruling did not impact claims 2 through 6 of the '723 patent. Under those claims, SmithKline retains the exclusive right to make and sell pure and pharmaceutically useful amounts of the hemihydrate (the active ingredient in Paxil®) in the United States. Claim 2 claims "[c]rystalline paroxetine hydrochloride hemihydrate in substantially pure form." *Id.* at 192a. Claim 3 claims the same compound as characterized by the results of several analytical chemistry tests. *Id.* Claim 4 claims a process for making the compound. *Id.* Claim 5 claims a pharmaceutical composition (*i.e.*, a tablet, capsule, etc.) containing an effective amount of the compound. *Id.* And claim 6 claims a method of using an effective amount of the compound to treat depression. *Id.* Hence, this lawsuit has never been about impairment of SmithKline's exclusive right to make and sell the hemihydrate; but it is very much about SmithKline's effort to prevent others from making and selling prior art paroxetine hydrochloride anhydrate.

SmithKline sought rehearing *en banc* from the Federal Circuit's inherent-anticipation ruling, arguing that waiver precluded review of the district court's rejection of Apotex's inherent-anticipation argument. *Id.* at 220a. The rehearing petition did *not* argue that the appeals court's decision conflicted with any of this Court's rulings. At any rate, the entire Federal Circuit denied rehearing *en banc* without a single dissenting vote. *Id.*